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3180

CONTENTS

Clinic of Dr. Henry A. Christian, *Peter Bent Brigham Hospital* PAGE

CHRONIC DIFFUSE PULMONARY EMPHYSEMA 1083

Clinic of Drs. George R. Minot and William P. Murphy, *The Collis P. Huntington Memorial Hospital of Harvard University and the Peter Bent Brigham Hospital*

LIVER DIET IN PERNICIOUS ANEMIA AND THE DISTINCTION BETWEEN ALEUKOCYTHEMIC MYELOID LEUKEMIA AND PERNICIOUS ANEMIA 1093

Clinic of Drs. William H. Robey and Louis M. Freedman, *From the Medical and Nose and Throat Clinics of the Boston City Hospital*

THE EFFECTS OF TONSILLECTOMY ON THE ACUTE ATTACK AND RECURRENCE OF RHEUMATIC FEVER 1103

Clinic of Dr. Frederick T. Lord, *Massachusetts General Hospital*

A CASE OF SPONTANEOUS SUBDURAL HEMATOMA IN WHICH THE DIAGNOSIS WAS MISSED DURING LIFE 1119

Clinic of Dr. Cyrus C. Sturgis, *Peter Bent Brigham Hospital*

ORGANIC LESIONS IN NEUROTIC PATIENTS 1131

Clinic of Dr. John Lovett Morse, *Professor of Pediatrics, Emeritus, Harvard Medical School*

ACUTE INFECTIONS OF THE NASOPHARYNX AND ITS ADNEXA IN INFANCY AND EARLY CHILDHOOD 1143

Clinic of Dr. Reginald Fitz, *From the Medical Clinic of the Peter Bent Brigham Hospital*

CLINICAL PROBLEMS IN THE MANAGEMENT OF DIABETES WITH A REVIEW OF FOUR FATAL CASES 1163

Clinic of Dr. Fritz B. Talbot, *Massachusetts General Hospital*

EARLY TUBERCULOSIS OF THE MESENTERY LYMPH-NODES. REPORT OF TWO CASES 1175

Clinic of Dr. Soma Weiss, *The Boston City Hospital*

THE CLINICAL ASPECT OF OBSTRUCTIVE DISEASES OF THE COMMON BILE-DUCT 1183

Clinic of Dr. Raphael Isaacs, *From the Medical Service of the Collis P. Huntington Memorial Hospital of Harvard University*

ANEMIA IN CANCER 1219

Clinic of Drs. Howard B. Sprague and Paul D. White, *Massachusetts General Hospital*

HIGH-GRADE HEART-BLOCK UNDER THE AGE OF THIRTY 1235

Clinic of Dr. Bronson Crothers and Margaret L. Wirt, A. B., M. S. S., *Children's Hospital*

THE MANAGEMENT OF MENTAL DIFFICULTIES IN A PEDIATRIC CLINIC 1251

Clinic of Dr. Clement I. Krantz, *The Medical Service of The Collis P. Huntington Memorial Hospital of Harvard University*

TWO CASES OF LYMPHOBLASTOMA WITH INCREASE OF BASAL METABOLIC RATE 1263

Clinic of Dr. Joseph T. Wearn, *From the Fourth Medical Service of the Boston City Hospital*

THE VALUE OF RENAL FUNCTION TESTS IN THE DIAGNOSIS OF EARLY NEPHRITIS 1273

Clinic of Drs. Elliott P. Joslin, Howard F. Root, and Priscilla White, *New England Deaconess Hospital*

DIABETIC COMA AND ITS TREATMENT 1281

Clinic of Dr. Henry Jackson, Jr., *Boston City Hospital*

THE PROGNOSIS OF CHRONIC NEPHRITIS 1307

Clinic of Dr. Maurice Fremont-Smith, *Boston City Hospital*

ON CERTAIN DIAGNOSTIC DIFFICULTIES IN PRIVATE CASES 1317

Clinic of Dr. Lewis Webb Hill, *Children's Hospital*

GLUCOSE AND INSULIN IN THE TREATMENT OF RECURRENT VOMITING 1329

OVERFEEDING WITH MILK (MILCHNÄHRSCHADEN "BILANZSTÖRUNG") 1339

Clinic of Dr. Edward S. Emery, Jr., *Peter Bent Brigham Hospital*

THE SIGNIFICANCE OF SO-CALLED CONSTIPATION 1345

Clinic of Dr. Roger I. Lee, *New England Deaconess Hospital*

THYROID DYSFUNCTION AS A CAUSE OF FEVER 1353

Clinic of Dr. Channing Frothingham, *Peter Bent Brigham Hospital*

A CASE OF CORONARY THROMBOSIS 1357

Clinic of Drs. W. Richard Ohler, and Louis J. Ullian, *Boston City Hospital*

MILD HYPOTHYROIDISM—PERSONAL OBSERVATIONS 1369

Clinic of Dr. Franklin W. White, *Boston City Hospital*

THE HEALING OF GASTRIC ULCER 1383

THE MEDICAL CLINICS
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NORTH AMERICA

Volume 10 No. 5

CLINIC OF DR. HENRY A. CHRISTIAN

PETER BENT BRIGHAM HOSPITAL

CHRONIC DIFFUSE PULMONARY EMPHYSEMA

TODAY I am presenting a patient whose prime features are shortness of breath and cyanosis.

OUTLINE OF HISTORY PRESENTED BY A MEDICAL STUDENT.—"This patient (Med. No. 27,811) is sixty-three years of age, a Polish Jew. He came into the Hospital on April 26, 1926, complaining of shortness of breath. His family history is essentially negative, except that his father died at the age of forty-two of a 'chest cold.' He is a merchant and has a men's clothing store. He has been in that business for thirty-two years. The only possible health hazard is that his store has gas heat. In his past history he had typhoid fever forty years ago, and he has had some 'lung infection' in the past ten years. For ten years he has had nocturia once or twice a night. His present illness dates back to about ten years ago, when he started having chest colds, which he describes as attacks of bronchitis or attacks of asthma. They are characterized by shortness of breath, cough, yellowish sputum, and quite severe headaches. These come especially in the spring and autumn months of the year and have been getting progressively worse with increasing shortness of breath. The present attack started early in March of this year, when he came down with a quite severe chest cold, and he had severe coughing with a great amount of yellow sputum. He also noticed severe shortness of breath on slight exertion. He took his work easily, but did not seem to get any better, and so sought medical at-

tention. Two or three weeks before entry into the hospital he noticed that his legs and ankles began to swell, and that his shortness of breath got worse, so that moderate exertion made him very short of breath."

The patient's main complaint is shortness of breath and cough. This goes back over a period of ten years. What I wanted you to notice particularly is his color. There is a striking cyanosis of his face, and there is marked cyanosis of his hands. In addition, I wish you to notice the type of his respiration. He is breathing rapidly, but he is not particularly uncomfortable with his difficulty in respiration. There is a certain amount of dyspnea, but it is more a rapid than a difficult respiration.

DR. CHRISTIAN (to patient): How is your color now, Mr. S., as contrasted with that of two years ago? Has it changed much?

ANSWER: No, very little.

That is probably a correct answer. He has had this cyanosis, I have no doubt, for a considerable part of this long period of shortness of breath, which, you will recall, he said began ten years ago. Just when it began I have no way of knowing, but I suspect he is not much more cyanotic now than he was one, two, or three years ago, at a time when he was working and going about with a certain degree of activity. That is a feature which I wish to emphasize. There has been marked cyanosis, probably over a considerable period of time, and it is disproportionate to his ability to undergo physical activity. I do not mean that he does not get short of breath when he moves about, but that the shortness of breath does not bother him a great deal. He is much more cyanosed in proportion to his degree of shortness of breath than most patients, and he can do more in a physical sense than most patients with his degree of cyanosis.

If you will recall his story you will remember that he had this shortness of breath and cough over a long period of time, but it is only just recently that he has shown any evidence of edema. In the last few weeks some edema has developed in his legs. According to his story he looked last year about as he does now; that is, he was as cyanosed as he is now and almost as

short of breath, but last year he had no edema of his legs, and never had had any prior to recently.

As you look at the patient in addition to noting his cyanosis and his rate of respiration, I want you to note particularly the shape of his thorax. You will see that there is a tremendous increase of its anteroposterior diameter, which is particularly well shown when you look at him laterally as I turn him around. You can actually see that his spinal column is curved, so to speak, around his thorax; that is, his spinal column is curved with the concavity anterior and the convexity posterior. You will also note that the sternum in front is somewhat curved, but in a reverse direction to the spine behind. This increased depth of his chest, with the curvature of his spine, as already noticed, gives him a peculiar appearance as if his head were set low between his shoulders on a very short neck, so that his neck and head are bent forward. If your ask him to raise his head, so that his chin is on a level parallel to the floor, you will see that he actually has to throw his head backward on his neck.

When you percuss the chest you will note that the lungs give a very markedly hyperresonant note, and when you listen you will find that his breath sounds are not very loud. Expiration is perhaps a little longer and it is certainly somewhat louder and higher pitched than inspiration, but the striking thing is that the whole sound picture of the lungs is a decreased one, and you have the feeling that there is a very definite disproportion between the size of his chest and its resonance, on the one hand, and the sounds that you hear on the other. A few scattered râles are heard. Just at present they are few. At times they have been more numerous; at other times absent. The râles that we have heard have been, in the main, medium-sized crackling râles.

When you come to the cardiac condition you find that he has a definitely enlarged heart. The apex is well out beyond the left nipple line. His lungs, being hyperresonant, interfere somewhat with percussing out the exact borders of cardiac dulness, but the area of cardiac dulness is certainly enlarged, extending well outside the nipple line. The heart sounds are per-

fectly regular in rhythm, at present not rapid. In ratio to his respiratory rate they are rather definitely slow, or to put it another way, his respiratory rate is increased out of proportion to his cardiac rate. The cardiac sounds themselves are not very loud, but you are hearing them through a good deal of pulmonary tissue. They do not seem to be abnormal in quality. There is possibly a very slight systolic murmur at the apex, no other murmurs heard. The blood-pressure was 150 systolic and 80 diastolic. The rest of his physical examination, except for the slight edema of the legs, shows no particular abnormality.

The condition is to be diagnosed as chronic diffuse emphysema of the lungs, with bronchitis, and, in addition, there are signs of moderate cardiac decompensation with evidence of a definitely enlarged heart. It seems to me that the increase in the size of the chest and its shape, with the condition of hyperresonance, with decreased intensity of breath sounds, can only mean voluminous lungs. These findings, in connection with the history that I have given you, seem to me to be very characteristic of chronic diffuse pulmonary emphysema.

As to whether you are to regard chronic diffuse emphysema of the lungs as a primary or secondary disease, there is a good deal of room for debate. It is a problem as to whether the lungs became overdistended first and the patient subsequently had recurring and persistent bronchitis as a result, or whether the patient had recurring and persistent bronchitis with cough and as a result pulmonary emphysema developed. It is possible, too, that the shape and size of the chest may play a part. I know of no way of determining the question. There is a definite pathology as far as the lungs are concerned in these cases, in that they have blown-up air-sacs and the air-cells are increased in size. Often quite large air-cavities seem to have resulted from adjacent air-cells or air-sacs becoming dilated and rupturing into each other. At least we get the appearance of partial subdivisions in these larger air-spaces which might easily have resulted in this way. With the distention of the air-sacs and air-cells their walls are decreased in thickness, and if rupture takes place the actual amount of wall between adjacent air-

spaces is decreased in amount. Both processes would work to interfere with respiration. The stretching and thinning of the air-sacs leads to a smaller bed of blood being brought into contact with the air within the lung, and the rupture further decreases the area of such wall. Both processes would hinder the satisfactory interchange of oxygen and CO_2. If to this is added bronchitis with moisture or exudate in the terminal bronchi, one would naturally expect to get a considerable degree of cyanosis. It is this cyanosis which is a very striking feature of many of these cases. When there is no or very little cardiac disturbance these patients, though markedly cyanotic, are not very uncomfortable and can carry on a very considerable degree of activity. In this respect they differ from the cyanosis of cardiac disease which is rarely so extensive without the patient being greatly limited in his activity. In cyanosis of cardiac origin cardiac therapeutics usually greatly improve the condition. In the cyanosis of pulmonary emphysema cardiac therapy has very little effect; its effect is proportionte to the amount of associated cardiac disturbance.

As already stated, it is uncertain as to which of these two processes, bronchitis or emphysema, was present first. On the whole it seems to me that it is more probable that the pulmonary lesion began before the bronchitis develops. This view is based on the observation that one frequently sees patients with a voluminous hyperresonant chest with little or no evidence in history or physical examination of bronchitis. As time goes on bronchitis becomes a very prominent factor. Then one sees many patients with a long history of bronchitis in whom the evidences of pulmonary emphysema are relatively slight or even entirely lacking.

Though there is this uncertainty in regard to which comes first, emphysema or bronchitis, it seems to me entirely clear that the cardiac decompensation is a late development of these cases, and all of the evidence is in favor of the cardiac hypertrophy and subsequent cardiac failure being a process secondary to the pulmonary emphysema and bronchitis. One might look upon the cardiac disturbance in these cases in very much the

same light as one looks upon the cardiac failure in patients with hypertension. In the one case the increased resistance or disturbance is in the pulmonary circulation, and in the other in the systemic peripheral circulation. In both of these conditions we do not know how much the cardiac enlargement is directly the result of increased vascular resistance, or how much it is due to some disturbance in the heart muscle from changes in the heart muscle itself or its capillary circulation. We know that in most patients with hypertension, as time goes on, there develops evidence of organic vascular lesion and cardiac hypertrophy with failure in function. It is also true that in these patients with emphysema that the pulmonary circulation is apt to show evidence of organic vascular lesion, and that, as time goes on, there is cardiac hypertrophy, and eventually cardiac failure. As I have observed some of these patients with pulmonary emphysema, it has seemed to me that, in contrast to those with hypertension, at first the right side of the heart shows disproportionately greater enlargement with subsequent hypertrophy of the left ventricle.

Apart from these patients with such marked evidence of chronic diffuse pulmonary emphysema, we see a great many patients who give the story of recurring attacks of bronchitis, often in the form of so-called winter colds, who run much the same course as has the patient that I am showing today. In them shortness of breath develops with bronchitis, which gradually becomes more marked. At first dyspnea is periodic, then its periods lengthen, and finally it becomes continuous. Somewhere at about this time the type of respiratory disturbance changes and the patients have periods of paroxysmal dyspnea, or without paroxysmal dyspnea the shortness of breath becomes very much more marked. Both types of dyspneic bronchitic patients at about this time begin to show some swelling of the legs, and from then on they progress as patients with cardiac failure. The first part of their story is dominated by the pulmonary disturbance, and the latter part of their story by the symptoms of cardiac decompensation. Of these patients, those with most marked emphysema show the most evident cyanosis.

Apart from cyanosis from chronic diffuse pulmonary emphysema, there are some other disturbances with cyanosis in which the patient will be found up and walking about. These are: (1) polycythemia cases; (2) patients with some chronic poisoning that gives a methemoglobinemia, and (3) an occasional patient with congenital heart disease.

Although this patient which I am showing has had cyanosis for a long time there is no very marked clubbing of the fingers. He has a little clubbing of his fingers, but it is not very evident. This is a curious thing. Why does not this patient who has had so marked a cyanosis not have more marked clubbing of the fingers? Some other type of cyanosis, particularly that of the congenital cardiac case and certain patients with very little cyanosis, such as patients with chronic bronchiectasis, have very marked clubbing of the fingers. Possibly the usual explanation of clubbing of the fingers, namely, anoxemia, explains the difference. Anoxemia and cyanosis are not necessarily coincident processes.

Some clinicians question whether one is justified in making a diagnosis of chronic diffuse pulmonary emphysema or not. They are inclined to the view that it is not a justified diagnosis. It seems to me that in a patient of this type, as just shown, one cannot escape from making that diagnosis. I believe that in a patient with this sort of history and these findings, that a postmortem examination would confirm the diagnosis of this type of pulmonary emphysema. To check up our accuracy at the Peter Bent Brigham Hospital in making the diagnosis of pulmonary emphysema I have looked up those patients during the period 1918–1925 in whom the diagnosis of pulmonary emphysema was made clinically and who subsequently died and came to autopsy, as well as those patients in whom the pathologist at autopsy had made a diagnosis of pulmonary emphysema.

Twenty-four cases fulfilling these conditions were found. In 4 of these the clinical and pathologic condition was lobar pneumonia and the pathologist described and diagnosed an acute compensatory emphysema. Fairly these may be excluded from the group under discussion. From the remaining cases, 20 in

number, 2 more may be excluded as scarcely belonging in the group under consideration, namely, the group of cases in which there is generalized chronic pulmonary emphysema, inasmuch as in 1 of these the emphysema was localized to a small area at the apex associated with a localized chronic tuberculosis; and in the other, though the emphysema was much more extensive, it was associated with bronchiectasis in a patient who had multiple aneurysms of the aortic and pulmonary arteries. Deducting these we have 18 patients who at autopsy showed varying degrees of chronic diffuse pulmonary emphysema.

Of 18 patients diagnosed diffuse pulmonary emphysema either in the clinic or at postmortem, 8 showed this condition to a marked degree when examined at autopsy. In 6 of these a clinical diagnosis of diffuse pulmonary emphysema was justified by a history and physical examination in general resembling that of the patient described in the first part of this discussion. In 2 of the patients with extensive pulmonary emphysema found at autopsy nothing in the history or physical examination was found to cause one to suspect this condition in the lungs. However, it is fair to say that both of these patients, in whom emphysema was not diagnosed during life, came into the hospital extremely ill and died within twenty-four hours after admission and consequently presented little opportunity for thorough physical examination. In a group of 4 patients in which the pathologist found only rather slight degrees of diffuse pulmonary emphysema, clinical study had seemed to justify a diagnosis of emphysema. Possibly here the pathologist's attention at autopsy was somewhat diverted or the emphysema was obscured by bilateral hydrothorax present in 2 of these patients, and a patchy bronchopneumonia in a third. In another 4 patients of the group nothing on the clinical side could be said to suggest emphysema; yet the pathologist found emphysema present in the lung, though not in a marked degree. Finally, in 2 patients in whom a clinical diagnosis of emphysema seemed fully justified, the pathologist found nothing to confirm this diagnosis, and so the clinical diagnosis was clearly incorrect.

It seemed to me that this experience with patients diagnosed

as having chronic diffuse pulmonary emphysema, and later studied pathologically, indicates about as good correlation between clinical diagnosis and pathologic findings as holds for a large proportion of diseases in which one is confronted with diagnosis of a condition which has varying stages of progression. It is hardly to be expected that a lesion of the type of diffuse pulmonary emphysema would be diagnosable clinically in the earlier stages of the development of the changes in the lungs, and it is reasonable to suppose that the pathologist would find the lesion present to a slight or even moderate degree when the clinician had failed to find evidences of it. Our experience with this relatively small group shows that in 6 of 8 patients with marked emphysema of the lungs clinical study had justified the diagnosis. In the two failures opportunity for clinical study was very slight. In 8 patients the pathologist found slighter degrees of emphysema; half of these were missed clinically. Two patients diagnosed clinically as having diffuse chronic pulmonary emphysema failed to show the lesion at autopsy.

The patient shown today represents a marked degree of chronic diffuse pulmonary emphysema with bronchitis and with a more recent development of cardiac failure, in my opinion secondary to the pulmonary and bronchial disease. With the appearance of signs of cardiac decompensation prognosis of continued life is much poorer, and it seems probable that this patient will have temporary improvement in his circulation with relatively early relapse and death before a great length of time has elapsed. The poor prognostic outlook is dependent in the main on the evidence of circulatory disturbance obtained in our clinical study of the patient.

CLINIC OF DRS. GEORGE R. MINOT AND WILLIAM P. MURPHY

THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL OF HARVARD UNIVERSITY AND THE PETER BENT BRIGHAM HOSPITAL

LIVER DIET IN PERNICIOUS ANEMIA AND THE DISTINCTION BETWEEN ALEUKOCYTHEMIC MYELOID LEUKEMIA AND PERNICIOUS ANEMIA

LIVER DIET IN PERNICIOUS ANEMIA

IN May, 1926, we reported[1] upon the beneficial effect of a special diet, one particularly rich in liver, for patients with pernicious anemia. Our experience from observations on over 70 practically consecutive cases now leads us to believe that the daily ingestion of a relatively large amount of mammalian liver (calves preferable) can increase very markedly and promptly the red blood-corpuscles of essentially all patients with pernicious anemia when the count of their red blood-corpuscles is low. These patients have been strikingly improved in health. Some have regenerated their red blood-cells faster than others, but an increase from approximately 1,500,000 to 3,000,000 per c.mm. in about four weeks has been the rule. The rate of increase becomes slower as the red blood-cell count rises. About two months after the diet has been begun the red blood-cells are usually 4,000,000 or more per c.mm. When the marrow has been severely affected by a great number of transfusions of blood perhaps it cannot respond satisfactorily. The pronounced symptoms and signs due to spinal cord degeneration remain present. Even so, in some cases the improvement in symptoms and signs referable to disorder of the central nervous system has been rather unusual and gratifying to the patient.

[1] Trans. Assoc. of Am. Phys., 1926, and Jour. Amer. Med. Assoc., 1926, 87, August 14th, 470.

The daily requirements of the special diet have been stated[1] as follows:

1. Liver (calves', beef, chicken) or kidneys (lamb) freshly cooked. At least 120, preferably 200 or more, grams (cooked weight). Cook without fat; broil, bake, boil, mince, or make into soup.
2. Fruits, preferably fresh—especially peaches, apricots, pineapple, strawberries, oranges, and grapefruit—about 400 grams. Raisins desirable; allow them to be eaten freely.
3. Red muscle meat, trimmed free of fat, freshly cooked; 100 grams or more. Beef heart desirable.
4. Vegetables containing 1 to 10 per cent. of carbohydrate, preferably fresh; cooked or raw. Not less than 300 grams. Lettuce, spinach, asparagus, cabbage, and tomato are especially desirable.
5. Fats restricted, not over 70 grams. Avoid cheese, bacon, fried food. Allow but little cream and butter, and not over one egg. Use mineral oil for salad dressings.
6. Avoid grossly sweet foods, yet allow sugar sparingly.
7. Starchy foods, as cereals, potato, breads, add to suit individual desires, but not to exclusion of the requirements given above. The starchy foods best be crusty or dextrinated. Whole wheat toast is desirable.
8. Milk best be limited to about 240 grams.
9. Avoid excess of salt. Tea and coffee as desired.

Ideally all food should be weighed. The liver is essential and must be weighed at first. After the patient understands the approximate quantity of the different foods to be taken, their amounts may be estimated.

When the patient is unable to take much food, it is important that he eat some liver and fruit, even if no other food be taken. Then gradually add meat and green vegetables. The starch foods are to be given in accordance with the amount of the other foods eaten. The patient should be expected to take the full diet within about two weeks after commencing it.

Present information suggests that the patient should continue with this sort of diet, even though his red blood-cell count remains high. How long the remissions of the disease are to last in patients that eat liberally of liver cannot be told as yet.

There is evidence that liver alone is the essential requisite of the diet to promptly enhance desirable blood formation.

[1] Boston Med. and Surg. Jour., 1926, 195, August 26th, 410.

It would seem as if this organ contained one or more constituents that permitted the masses of megaloblasts in the marrow to maturate, perhaps to supply stroma material which has been thought to be lacking (Whipple). Although ordinary cooked liver is effective, evidence to be reported on later suggests that raw liver served after being ground up into pulp has an even more potent effect. If necessary the liver may be given through a stomach-tube.

Recent tests indicate that a large amount of fat in the diet may not inhibit the blood formation, but there remain theoretical reasons why it may be best to keep it relatively low. Fruits, red muscle meat, and green vegetables may be classed as desirable foods for the patients, but improvement may be expected even though these foods are not eaten. The more concentrated starch foods exert no useful influence on blood formation. Milk probably tends to cause constipation, and the grossly sweet foods often favor an acid fermentation in the colon so common in these patients with achylia or achlorhydria.

This diet can benefit other cases of anemia than those of pernicious anemia, but certainly not all. There are forms of severe anemia that may simulate closely pernicious anemia. The absence of alleviation of anemia in such patients by ingestion of large amounts of liver might cause one to believe that it had failed to benefit a case of pernicious anemia. The following case that we present to you illustrates how this might occur on account of an erroneous diagnosis.

DISTINCTION BETWEEN ALEUKOCYTHEMIC MYELOID LEUKEMIA AND PERNICIOUS ANEMIA

The patient is a man fifty-four years of age, who appears obviously pale and perhaps slightly sallow. He has white hair that used to be black and very dark colored eyes. He weighs 190 pounds, and is 5 feet 10 inches tall. Addison wrote in 1856 that pernicious anemia occurs "chiefly in persons of a somewhat large and bulky frame and with a strongly marked tendency to the formation of fat." Recently Draper has studied the anthropologic make-up of patients with pernicious anemia

and has shown them to approach in type a person with hyperactivity of the pituitary gland, to have wide facies, eyes set far apart, wide jaw, and costal angles. This patient has these features noted by Addison and Draper as rather characteristic of individuals who suffer from pernicious anemia. People with this disease are apt to have light-colored or white hair as this man has, but, unlike him, they are prone to have blue or light colored eyes. The fact that his irides are dark does not, of course, rule out pernicious anemia.

His past history and family history give no information that need concern us except for his dietary habits and gastro-intestinal symptoms. He has eaten always excessively of bread and has been throughout life exceedingly fond of butter, cheese, and cream, so that it was not unusual for him to eat over 160 grams of fat a day. He has seldom eaten green vegetables, almost never salads, and fruit only sparingly. The animal protein foods have been taken in moderate amounts, but all forms of starch foods and sweets have been consumed in large quantities. It has been our experience to note that frequently patients with pernicious anemia have partaken of an abnormal diet for many years before symptoms of anemia appear, and not a few have tended to choose their food in the manner that this patient has. Data concerning this will be reported upon subsequently. However, because this patient has eaten abnormally, it is no reason in itself to lead one to the diagnosis of pernicious anemia.

Throughout life he has been constipated and frequently made uncomfortable by excess of intestinal gas. Occasionally attacks of vomiting without distinct pain have occurred in the past six years.

Two or more cases of pernicious anemia in one family are not unusual. Such information when of a positive sort may be of value in aiding diagnosis, but when negative, as for this patient, carries no significance.

Seven months ago this man had a mild attack of bronchitis. The symptoms of bronchitis vanished within two weeks. Since then, however, he has grown progressively weaker, gradually developed shortness of breath on slight exertion, has felt rest-

less, slept poorly, and within the past few weeks has developed ill-defined recurrent transient pains about his ribs, sternum, and thighs. Other common minor symptoms chiefly referable to the gastro-intestinal tract have occurred. He now weighs 15 pounds less than seven months ago.

He has suffered from no symptoms suggesting a glossitis or disease of the central nervous system, symptoms that are classical of pernicious anemia. Likewise physical examinaton reveals no atrophy or lesions of the tongue, nor any evidence of a disorder of the central nervous system. A tuning-fork is often of great value in helping to decide whether pernicious anemia exists or not. Its use is apt to be neglected. The vibration sense (bone conduction) is tested by simply placing a vibrating tuning-fork on different parts of the extremities and determining how long the vibrations can be felt. Diminution of this sense is very common in pernicious anemia and is often the earliest demonstrable sign of spinal-cord involvement and sometimes can be detected as decreased before the patient is aware of any definite central nervous system symptoms. The absence of symptoms or signs referable to a glossitis or the central nervous system does not rule out pernicious anemia, but should make one cautious in establishing that diagnosis.

Some weeks ago his stomach contents were analyzed only thirty minutes after a test-meal of bread and water. No free hydrochloric acid was found. It is our belief that a total lack of free hydrochloric acid in the stomach contents is a constant feature of the disease, pernicious anemia. However, one test alone made but thirty minutes after a test-meal does not establish this. A study should be made of a series of samples of gastric contents obtained at intervals of fifteen to thirty minutes for from one and a half to two hours after a test-meal, to demonstrate the absence of free hydrochloric acid in the gastric secretion. This test has recently been made. There was no free acid at the end of half an hour, but in each of 5 samples obtained from forty-five minutes to two hours after the test-meal free acid was present, although in quantities distinctly less than normal. Thus the presence of free hydrochloric acid is at least very strong

evidence that the patient has not pernicious anemia, and in our opinion rules out that disease.

Five weeks ago the blood examination showed: Hemoglobin 50 per cent., red blood-corpuscles 2,200,000 per c.mm., and they appeared of a type consistent with those seen in pernicious anemia, although macrocytosis was recognized as distinctly slight. A nucleated red blood-cell was rarely observed.

The blood-platelets were considerably diminished.

The white blood-cells were 4400 per c.mm.

Their differential count has been recorded as follows:

	Per cent.
Polynuclear neutrophils	29.5
Polynuclear eosinophils	1.0
Polynuclear basophils	0.5
Myelocytes	2.0
Myeloblasts	7.0
Lymphocytes	50.0
Monocytes	10.0
	100.0

When this differential count of the white blood-corpuscles was first made the myeloblasts were called lymphocytes and the myelocytes called monocytes, so that it as well as the rest of the blood examination was considered consistent for a case of pernicious anemia in relapse. It is, however, very probable that more than 7 per cent. of myeloblasts occurred, because, we believe, some of the cells recorded as lymphocytes in the table above were atypical small myeoblasts.

During the past five weeks the patient has eaten daily between 170 and 280 grams of cooked liver and has taken generously food of the sort contained in the diet we have advised for patients with pernicious anemia. However, he has improved in no way except that now he passes daily regular formed stools and has fewer digestive symptoms than formerly.

His temperature was normal three and four weeks ago. For two weeks it has been between 98° and 101° F. in the morning, and at least 101° F. and recently often 102° F. in the evening. His pulse rate has been about 110 beats per minute. Pernicious

anemia may cause fever, but we have observed no such degree of fever due to the disease as this patient has had in patients with pernicious anemia who have eaten large amounts of liver for three weeks.

The intermittent sense of lameness about the ribs, sternum, and thighs has perhaps increased in the past two weeks. This has not been marked. Pain or discomfort is produced by pressure upon the sternum. Roentgen-ray examination of the bones of the thorax and femurs reveal no abnormalities. Many questions have been asked the patient and no further significant information has been obtained from him or his relatives than that given above.

No cause has been found for the patient's fever except the fundamental disease of the bone-marrow that he has. The symptoms referable to the ribs and sternum are ones that occasionally occur in such cases.

Complete physical examination has revealed besides his abnormal appearance, fever, and tenderness over the sternum only the following abnormalities: A systolic murmur over the precordium believed dependent upon his anemia; clusters of fine petechiæ over his lower legs, which are associated with the marked reduction of blood-platelets. In the groin there are a few very small palpable lymph-nodes, but no larger or in greater numbers than are found in many healthy persons. The lower liver edge can just be felt on deep inspiration, but the spleen is not palpable. The urine, stool, and various laboratory tests, except those of the blood, have revealed no significant abnormality. No Bence-Jones "bodies" occurred in the urine.

The blood examination today establishes the diagnosis. The hemoglobin 40 to 45 per cent., red blood-cells 1,800,000 per c.mm. They show a marked variation in size, and inspection of the blood-smears suggests a slight general macrocytosis to be present. However, actual measurements of the diameters of the red blood-corpuscles show that their mean diameter is at the upper normal limits. In pernicious anemia in relapse the mean diameter is practically always distinctly greater than normal. True microcytes of the type associated with blood de-

struction occur in his blood, but are rare. Variation in the shape of the red blood-cells is present, but is not marked. The cells take the stain about as deeply as normal cells do. There rarely occurs a polychromatophilic cell, and the reticulocytes are 1.5 per cent. Nucleated red blood-corpuscles are very rarely observed.

It has been reported to us that there was no definite increase in the reticulated red blood-cells within twelve days after the patient began eating liver. This is in sharp contrast to what pernicious anemia patients usually have shown. Their reticulocytes have, as a rule, increased promptly and considerably—usually to 10 per cent. or more and even to 50 per cent. within a few days after starting to take large amounts of liver.

The blood-plasma appears slightly yellow, and its bile-pigment content is a little greater than normal as shown by an icterus index of 7. It is distinctly unusual not to find the icterus greater than this in cases of pernicious anemia with red blood-cell counts of 2,500,000 per c.mm. or less. The pigment increase in pernicious anemia plasma has been associated particularly with abnormal red blood-cell destruction which many have considered a primary process of the disease. There are good grounds for the belief that in pernicious anemia the typical increase of hemoglobin derived pigments in the blood and tissues is a secondary manifestation resulting at least partially from the absence of red blood-corpuscles to make use of them. The primary disease process in pernicious anemia would appear to be located in the bone-marrow as originally suggested by Cohnheim in 1876, and referred to above as an inability of the megaloblasts to maturate properly.

The patient's blood-platelets are very markedly reduced and some are abnormally large. It is the rule, of course, to have these elements few in the blood-stream during a relapse of pernicious anemia, but seldom are they very markedly reduced, although this is common in the advanced stages of this patient's disease.

The white blood-cells are 7000 per c.mm.

Their differential count is as follows:

	Per cent.
Polynuclear neutrophils	5.3
Polynuclear eosinophils	0.3
Polynuclear basophils	1.0
Myelocytes	2.3
Monocytes	1.1
Myeloblasts	90.0
	100.0

The myeloblasts might have been mistaken for ordinary lymphocytes if careful scrutiny had not been given these cells. They are chiefly pathologic in type and small in size, with often multiple nucleoli. The nucleoli in practically all were clearly visible and pale, not dark, in color. Some might consider that these immature cells were lymphoblasts, but the essential point to recognize is that they are obviously very immature pathologic cells occurring in relatively great numbers in the peripheral blood.

This blood-picture indicates that the patient has a rather unusual form of leukemia—an aleukocythemic, myeloid, or myeloblast leukemia or myeloblastoma—a condition that probably often has been mistaken for pernicious anemia. The marked decrease of red blood-corpuscles and blood-platelets is to be explained by a crowding out of their parent cells in the marrow by these tumor-like cells—myeloblasts—somewhat similar to pernicious anemia in relapse when there occurs in the marrow an abnormal growth of megaloblasts.

Unusual cases of primary bone-marrow disease that are not pernicious anemia occur without a distinctive blood-picture, such as did develop in this case. Some of them are cases of myeloblastoma of a type known as aleukemic myelosis with extensive proliferation of myeloid tissue and at times many nucleated red blood-cells in the peripheral circulation; others have been grouped with cases of idiopathic thrombopenic purpura. Cases of myeloblastoma with a low white blood-cell count and with either a distinctive leukemic or non-distinctive aleukemic white blood-cell picture are some of the ones that may be incorrectly diagnosed as pernicious anemia.

This patient died four weeks later. The blood-picture during the last weeks of his life remained essentially the same, although the hemoglobin percentage and red blood-cell count fell to lower figures. It is to be noted that his disease showed no tendency to remit, although rather brief periods of some, but not marked, improvement may occur in such cases. It is most unusual for a patient with pernicious anemia to steadily decline to death. At least one remission of some degree nearly always occurs in pernicious anemia, so here again is a distinction between pernicious anemia and the disease this patient had.

CLINIC OF DRS. WILLIAM H. ROBEY AND LOUIS M. FREEDMAN

FROM THE MEDICAL AND NOSE AND THROAT CLINICS OF THE BOSTON CITY HOSPITAL

THE EFFECTS OF TONSILLECTOMY ON THE ACUTE ATTACK AND RECURRENCE OF RHEUMATIC FEVER*

RHEUMATIC[3] heart disease has become the most important condition affecting the immediate and subsequent health of young individuals. Its great cause of mortality in early life, its economic losses during the earning years, and its probable effect upon the heart muscle of older adults, raises it to a position demanding the study of all physicians.

Heart disease as a cause of death in the aged seems to us at present the ultimate result of a worn-out mechanism, but how much this destruction is due to early infections and how much to wear and tear, is as yet an unanswered question. The goal to be attained is the discovery of the specific organism of acute rheumatic fever. Whether there is a specific organism, or a combination of the already known bacteria, is the problem. It is not the purpose of this paper to discuss the bacteriologic problem; the literature of the day attests the increasing interest which physicians are showing in this question. In the meantime, is there anything we can do to diminish rheumatic infection in the young, and its insidious areas of degeneration in the old?

Focal infection has been extensively studied and written about in recent years, and the eradication of foci has been used to clear up a variety of disabilities. The wholesale enucleation of tonsils for many conditions, often without thorough study of the cases, has done much to make physicians skeptical of the

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value of tonsillectomy. Many good medical and surgical measures have been stampeded in an effort to make them cure-alls, and in the rush the real value has been lost sight of.

It is highly essential that we should have clearly in mind the symptoms and signs of acute rheumatic fever, differentiating the types seen in children from those of adults.

In children and young adults we have the rheumatic and infectious group, in middle life the results of early heart infections, including syphilis and arteriosclerosis, from whatever cause, and in the old age group the general breaking down of the circulation, with frequent involvement of the coronaries.

In this particular discussion we are concerned only with rheumatic heart disease, its causes so far as they are known, and its far-reaching results. We have, therefore, to consider primarily the young age group. Years ago physicians concerned themselves too much with declared cardiac lesions, their correct diagnosis, and appropriate treatment. All this, of course, is still necessary and will continue to be throughout the life of all here and for a long time after we are gone, but we hope in a much less degree. The physician of today is not doing his duty to himself and his patients unless he regards every child as a case of *potential heart disease*. Unless we consider every child in our practice in this light, we are merely waiting to treat ultimately the one serious and crippling manifestation of rheumatic fever, viz., rheumatic heart disease. Once the child has entered this class he looks forward to limited usefulness and eventually to hopeless invalidism.

If we base our conception of rheumatic fever on the adult type we will go far astray in recognizing many of its important manifestations in childhood. The common type with fever, hot, tender, and swollen joints, the inflammation moving about from day to day, is not seen so frequently as it was twenty-five years ago. Rheumatism is a loose and general term applied by the laity, and too often by physicians, to any muscular or joint discomfort.

Cardiologists are interested in rheumatism as an infectious disease which occurs in children and young adults. Sometimes,

as recently pointed out by MacCallum, with a very acute course, more often progressing slowly with several explosions of acute illness in which different symptoms may become especially prominent. Equal stress was laid upon this point by G. F. Still[1] in 1910, when he said that the conception of rheumatism as essentially a joint disease is based on its occurrence in adolescent and adult life; the wider, and almost certainly more accurate, conception of rheumatism as a general disease, probably of infective origin, is based chiefly on its manifestations in childhood. To measure the frequency of rheumatism in childhood by the number of cases which come under treatment for the articular manifestations is entirely to misunderstand the prevalence of the disease in early life. Often joint symptoms are so slight that comparatively few of the cases in which they occur come under medical observation until the presence of severe cardiac affection, or the more obtrusive phenomena of chorea, induce the patients to seek medical advice. How frequently we realize this when taking the past history of a young adult with cardiac disease; no history of joint involvement sufficient to cause attention can be elicited. When joints are affected they may be excessively painful, but we know that in rheumatic fever the joints differ from all other types of rheumatism in affecting the periarticular tissue and not being distinctive as are the joint changes in chronic arthritis, syphilis, tuberculosis, sometimes gonorrhea, and even scarlet fever. No constant bacterium has been found in the joint fluid and the pain subsides, leaving the joint apparently unchanged. Indeed, rheumatic fever in the young would be of negligible significance were it not for the frequent cardiac sequelæ.

The course of rheumatic disease varies so greatly that a physician may easily overlook the condition. It often begins in children with malaise, frequently with tonsillitis, soreness, or redness of the throat. There may be only a day or two of illness, perhaps a little effusion into a joint or the adjacent structures, or vague muscular pains. The whole course may be very insidious. There may be anemia, nervousness, and irritability which may quickly disappear. A careful physical examination

during or immediately after these manifestations may reveal a beginning murmur in the heart. The more marked cases are, of course, easy to recognize. A few run a very acute and virulent course, beginning with tonsillitis or sore throat, and may terminate from hyperpyrexia and acute pancarditis.

A source of great danger to the child's heart is the occasional attack of malaise accompanied by varying degrees of fever. The illness drags along for two or three weeks. A careful physical examination several times repeated fails to give objective signs, and unless the physician is wary he is apt to pass it as a case of unexplained fever. A few months later the circumstances are repeated. It is our experience that harmless looking tonsils are often the basis of these attacks. Some years ago a young woman on the medical service had a fever lasting three weeks. Typhoid was seriously considered, but one morning she complained of soreness of one of the tonsils—an enucleation followed, with almost immediate relief.

Rheumatic fever in Southern climates is comparatively rare, as are mitral stenosis and other rheumatic heart diseases. This was brought out in a canvas of the country with regard to the establishment of organized work in the prevention of heart disease. In Northern climates rheumatic fever is much commoner, especially in the British Isles, which probably have the greatest incidence. G. F. Still,[1] whose work in rheumatic heart disease in London is well worth studying, enumerates a large number of subjective and objective signs.

In this country we note particularly tonsillitis, joint and muscle pains, pleurisy, bronchitis, anemia, emaciation, fever, nervousness, irritability, chorea, skin eruptions, rheumatic subcutaneous nodules, and the various degrees of cardiac involvement. Still has a great deal to say about rheumatic nodules. They are always in the deep fascia, tendon, or periosteum. The skin is always freely movable over them. They are most frequently found over the olecranon, about the malleoli and patellæ, over the spinous processes of the vertebræ, along the superior curved line of the occiput, and on the extensor tendons of the forearms. They occur in successive crops and may remain

for a few days or many months (Boas). MacCallum thinks that they are rare in children and much rarer in adults. From our own experience we think cutaneous manifestations not so rare as nodules.

Chorea is no longer considered an entity, although it is often admitted to the neurologic services of hospitals, where it has no more place than the joints of acute rheumatism. MacCallum quotes C. F. Strong, who in analyzing a large number of cases found that 20 per cent. of patients with chorea had organic heart disease. He thought that recurrence of the chorea increased the probability of serious cardiac involvement, and found that when chorea and rheumatism were combined 70 per cent. of the patients had heart disease. The pathology of chorea is still very little known, but recent careful work seems to show that there are in the central portions of the brain, in the corpus striatum, the optic thalmus and the subthalmic region, perivascular infiltrations of cells, which in a sense suggest comparison with the lesions found in epidemic encephalitis. Of the remains of such lesions, after the disappearance of the symptoms, nothing is known. Treatment for chorea is the same as for acute joints—rest, salicylate of soda, and the removal of foci.

More than twenty years ago writers began to apologize for the introduction of discussions dealing with focal infections, rheumatic fever, and chorea. While the literature is indeed voluminous, the conclusions of many papers are doubtful and often unconvincing. When one approaches the subject today he feels as though he stepped from the trenches into No-man's Land. One author quotes from the extremists of both camps. At a meeting a physician stated that it was criminal negligence not to remove the tonsils from every child, and that there should be a law making it malpractice for a physician who refuses to carry out this part of his duty. On the other hand, another physician said, "Thank God, no one has yet succeeded in stealing my child's tonsils." Such radicalism displays a viewpoint resting on narrowness of vision.

Boas,[2] in an extensive article on rheumatic heart disease, says that many misguided enthusiasts tonsillectomize, as a matter

of routine, every patient with heart disease. He states that if the rules for tonsillectomy laid down by St. Lawrence were followed they would condemn every child to tonsillectomy. In the opinion of Boas, most tonsillectomies, whether on sufferers from heart disease or on others, are unwarranted. He considers the evidence that the removal of tonsils will prevent rheumatism is unconvincing. To make such a sweeping statement that most tonsillectomies are unwarranted is not in accord with the clinical experience of many of us.

Price[3] concluded from twenty years of rural practice that, "as a matter of fact, the operation is rarely necessary," and should be done only after the most painstaking examination to determine the necessity therefore.

Goldberger[4] stresses the importance of physical examination and states "children, whose catarrhal conditions of the upper air passages do not subside after tonsillectomy and adenoidectomy, suffer in all probability from accessory nasal sinus disease, the antrum being the most frequently involved sinus." We believe, with Goldberger, that the thorough physical examination is of vast importance; but that all other conditions should be found, or carefully ruled out, before tonsillectomy is performed. If one follows out the rule of thorough physical examination in every case before anything is done, an infected antrum would have been found before tonsillectomy.

While Hunt and Osman believe "that enucleation is not a certain preventive of a recurrence of rheumatic fever," to them it seems probable that although tonsils may be the primary focus of infection, or portal of entry, in the first attack, the infective agent may remain dormant in some other part of the body. Frequent recurrences in patients with heart lesions suggest that the persistent focus may be in the heart itself. One striking point is that Hunt and Osman say nothing about the importance of investigating their cases after tonsillectomy for complete enucleation.

One author who contends that tonsillectomy is generally useless quotes this report in substantiation of his views, but apparently overlooks the fact that Hunt and Osman clearly

state that the primary focus was probably in the tonsil. This report plainly upholds our viewpoint that in many cases the primary focus is not removed early enough, nor is it thoroughly enucleated.

Cohen[6] speaks of the dangers of operation. He had three deaths from local anesthesia, two of which were unexplained, one before, and one after, operation. He feels that it is impossible to discover the need of tonsillectomy by inspecting the tonsils, but that the history of each case is of great importance and should be studied from its own angle.

Absolute indications for tonsillectomy according to Cohen are: (1) Recurrent attacks of tonsillitis, whether of the suppurative or simple variety; (2) when the acute attack is followed by such complications as rheumatism or heart disease.

Alvarez[7] insists that tonsils must not be removed for trivial causes, nor until a thorough study of the case has been made by a competent internist. He gives a long list of diseases for which tonsillectomy was performed with the hope of alleviation, but, of course, with failure in many instances. It would be ideal if such an operation could relieve but a small portion of the diseases for which it has been tried, but it is folly to think that it could. No operation of any sort should be undertaken until the most exhaustive study possible has been made of a case, and this applies to tonsillectomy fully as much as any other.

St. Lawrence[8] studied the effect in 94 children of tonsillectomy on the recurrence of acute rheumatic fever and chorea, in a special children's cardiac clinic, and concluded that complete removal of the tonsils was the most important measure for the prevention of acute rheumatic fever and the allied rheumatic manifestations. One or more attacks of rheumatic fever had occurred in 42 cases before the tonsils were removed. After tonsillectomy there was no recurrence in 35 cases, or 84 per cent. One or more attacks of chorea had occurred before the removal of the tonsils in 40 cases, and there was no recurrence after operation in 20 cases, or 50 per cent. Fifty-eight cases of organic heart disease were present in the series. Twelve of these patients had suffered at least one attack of cardiac failure before the

tonsils were removed. One patient suffered one attack afterward.

Janeway[9] stated that he did not consider tonsillectomy a prophylactic panacea, indeed, he had grave doubts as to its usefulness after the patient had suffered an attack of rheumatic fever, but he did not allow these doubts to prevent the patient from receiving what benefit the operation might give.

Alexander Lambert, in 1000 consecutive cases of rheumatic fever at Bellevue Hospital, found that 25 per cent. were recorded as having septic tonsils and 22 per cent. inflamed throats, making a total of 47 per cent.

White,[10] in a series of 73 cases of rheumatic fever in American soldiers, found that 40 per cent. showed enlarged or ragged tonsils; while Pemberton, in 400 cases of aortitis, found the tonsils were the seat of infection in 52 per cent.

The interesting study by Kaiser[11] has received considerable attention and his observations upon the effect of tonsillectomy on rheumatism, chorea, and heart disease mainly prompted the writers' study. Kaiser concluded that tonsillectomy offers a child considerable relief from such common complaints as sore throats, head colds, and mouth breathing. Tonsillitis and sore throats were among the most common infections before operation. In the group not operated upon the incidence was about the same. However, during the three-year period following operation, the incidence was greatly decreased. Of the 1200 children not operated on, 677 complained of frequent attacks of sore throat, as against 64 of the tonsillectomized children. Frequent head colds were reported in 614 of the children not operated on; while in the same number of children operated on, 146 were still subject to frequent head colds. In Kaiser's conclusions he states that operation had not influenced the incidence of chorea and rheumatism, but had shown a lessened incidence of cardiac disease over a period of three years. Fifty-two of the 1200 controls showed heart disease, while in the group operated on there were 44 cases of heart disease, 31 of which existed before operation and only 13 developed after operation.

The British Ministry of Health published an extensive re-

port in 1924 on the incidence of rheumatic diseases. On page 60 the report discusses tonsillar sepsis as an etiologic factor in rheumatic diseases. Male patients of the age group sixteen to twenty-four, with acute rheumatism, showed tonsillar sepsis in 49 per cent.; and female patients of the age group sixteen to twenty-four, in 36 per cent.; male patients of the age group twenty-five to twenty-four in 38 per cent.; and female patients twenty-five to thirty-four in 50 per cent. In the male group sixteen to twenty-four, 18 per cent. more had frequent attacks of tonsillitis with normal appearing tonsils; and in the female group sixteen to twenty-four, 25 per cent. In the male group twenty-five to thirty-four, 25 per cent. more had frequent attacks of tonsillitis without abnormal appearance; while there were in the female group twenty-five to thirty-four, 5 per cent. These, added to the percentages of definite tonsillar sepsis swells the rôle which the tonsil plays in acute rheumatism. The report states that some allowance should, perhaps, be made for that natural bias which would tend to make a medical observer regard as abnormal in a patient with acute rheumatism, tonsils, which in another patient he might pass as normal. But with this reservation there is no mistaking the prominence of the evidence of tonsillar sepsis or the history of it in the case of acute and subacute rheumatism.

The present study was undertaken to see if any data of value could be gathered with special reference to the relation between tonsillectomy, rheumatism, chorea, and rheumatic heart disease.

It is our belief that if acute rheumatism and its sequelæ can be reduced, that rheumatic heart disease will be proportionally eliminated. We did not think it possible to find cases that had been in the wards of a large hospital longer than five years ago, although we realize that the longer periods give the most valuable information as to the results of tonsillectomy and its prevention of rheumatic fever. The patients were written to and invited to come to the hospital, where Dr. Freedman examined the oral and nasal conditions, while Dr. Robey went into the histories and examined the hearts. A few could not come to the hospital because of their occupations, or for other good reasons, but these were thoroughly investigated by our social worker.

We collected 910 cases, but of this number we were able to investigate only 454. Public hospital patients move so frequently that it is impossible to trace them, so that we were unable to see many who were patients in the hospital in the fifth and fourth years of the study period. In the shorter periods the numbers increased, but naturally their value in a study of this type lessened.

In the group of 910 cases only those were selected who were discharged from the hospital with a diagnosis of rheumatic fever or chorea. In this group were included a few cases of repeated attacks of tonsillitis and rheumatic heart disease. Any case not having a clear history of rheumatic fever or rheumatic heart disease was excluded. A few cases of arteriosclerotic heart were excluded, although a diagnosis of rheumatic fever had been made.

Total number of cases		910
Not found	456 or 50 per cent.	
Seen in clinic	217 or 47 "	
Investigated by social worker	197 or 44 "	
Dead (of cases investigated)	40 or 9 "	
Tonsillectomies		201
No tonsillectomies		253
Number to be considered in this study		454

Tonsillectomy

With no subsequent rheumatism nor chorea (Care of teeth advised in 7.)	139 or 31 per cent.
With subsequent rheumatism (Teeth possible focus in 6.)	45 or 10 "
With subsequent chorea	17 or 4 "
Total tonsillectomies	201

Note.—Included in above were 32 cases of poor tonsillectomy, with subsequent rheumatism in	9
With subsequent chorea	6
With no other attacks	17

No tonsillectomy

With no further rheumatism nor chorea	160 or 35 per cent.	
(Poor condition in 15.)		
(Tonsillectomy advised in 60.)		
With further rheumatism	50 or 10 "	
(Bad dentition in 24.)		
(Tonsillectomy advised in 17.)		
With further chorea	2 or 0.6 "	
(Both with rheumatic heart disease.)		
Radium treatments	1 or 0.4 "	
(No further attacks.)		
Dead—Heart conditions	25	
Other causes	15	
Total number of tonsillectomies	253	

Number of cases with rheumatic heart disease	185 or 41 per cent.	
Rheumatic heart disease after tonsillectomy	10 or 5 per cent.	
(Teeth focus in 1 case.)		
Rheumatic heart disease *before* tonsillectomy	93 or 50 "	
With no further attacks		71
With further rheumatism		14
(Teeth in 50 per cent. of these.)		
With further chorea		5
Dead		3
		93

Note.—Of these 93 cases there were 18 with tonsillar tissue remaining.

Lung abscess following tonsillectomy	1 or 0.5 per cent.	
Tonsillectomy during or just after attack with no subsequent attack	129 or 64 "	
Rheumatism immediately following tonsillectomy		14

Rheumatic heart disease with no tonsillectomy	82 or 43 per cent.	
With no further attacks		51
With further rheumatism		7
With further chorea		2
Dead		22
		82

Tonsillectomies have been performed by us on about 60 cases of acute rheumatic fever *during the height of the attack.* None were operated upon until all medical measures, such as full doses of salicylate of soda, diet, and rest, had been thoroughly tried, and until such measures had proved to be useless. The

fever had run much the same course—joint inflammations recurred and there was, as far as we could observe, no material improvement. The length of time from admission to operation varied from five to eight weeks. Some of these cases did not have rheumatic heart disease, while others entered with it, the result of previous attacks of rheumatism. Some of my hospital colleagues insisted that operation, if they are convinced that operation is necessary, should be deferred until the acute attack has entirely subsided.

Starling,[12] while working at the Colchester Military Hospital during the war, was much impressed with the frequent history of tonsillitis, both with and without rheumatism, in the various types of cardiovascular disease received there. He quotes L. F. Barker, who insists on the removal of enlarged tonsils in most cases of rheumatic heart disease, but who states that it should be done between, and not during, the attacks, since there is danger of throwing more cocci into the blood. Starling finds that sore throats, unless very severe or often repeated, make little impression upon the patient's mind, and are easily forgotten when reciting his history. He feels that tonsils are the main portal and focus of rheumatic infection, and that the presence of enlarged lymphatic glands under the jaw is a more constant proof of tonsillar infection than the appearance of the tonsils themselves. Starling advises enucleation as early in the infection as possible, so as to end the attack; for, as he says, "it must be remembered that the longer the attack lasts, the more extensive the results."

We have arrived independently at the same conclusion as Starling. The question of driving more cocci into the blood by tonsillar operation, the fear expressed by Barker, was thoroughly considered by us before beginning operative treatment. We had to decide whether it was wiser to take the risk, if there was any, of driving more cocci into the circulation, or of allowing an infection to continue week by week, with all its dangerous possibilities. It seemed to us that the danger of adding more cocci to a blood-stream already constantly carrying many of them was worthy of less consideration than some have given to it. To

stand by doing nothing while ordinary treatment failed, not knowing what moment a heart infection might begin, or when a heart already infected might become more seriously damaged, was like watching a building burn without effort to put out the fire.

We feel now that we should have operated much sooner than we did, but in any event not until we had thoroughly studied the case. We arrived at the decision as soon as we could satisfy ourselves, by examination and elimination, that the tonsils harbored the focus. We know that a number of cases will promptly quiet down under full doses of salicylate and bicarbonate of soda, combined with rest. This was a process of subduing rheumatic fever in use twenty-five years ago, but what happened was that often as soon as the patient's resistance was again lowered by his activities, mode of living, or both, the process returned. Very little attention was paid to foci of infection. Tonsils, sinuses, and teeth were ignored. Patients sometimes had as many as two or three attacks in a year.

Since we believe that repeated attacks of rheumatic fever only add to an already damaged heart, the operation is important. One could treat medically and thoroughly investigate a case in one week as well as four, and by such procedures be that much earlier in recommending a necessary tonsillectomy.

In these 60 cases we felt that the tonsils were without question the cause of the acute process, because in from two to three days it had quieted down following tonsillectomy. If the tonsils were not responsible why did the symptoms, which had persisted for weeks, quiet down so promptly, not to return? The hot, red, tender joints had continued with only a day or two of remission for weeks. In 2 cases of marked chorea, 1 was entirely relieved in forty-eight hours, the symptoms having been just as marked up to the time of operation. In the other, the symptoms slowly subsided until they disappeared at the end of ten days. These cases seen nearly a year later had had no return.

In the cases with the acute joints there was no instance where the inflammation was not promptly dissipated. There were no

complications, such as lung abscess or disturbances from the anesthetic. The patients accepted operation in most instances quite readily, because they were concerned about stopping their severe pain, while we were chiefly worried over the possibility of heart involvement. One woman with repeated recurrence of joint inflammation while in the hospital, delayed the operation for two days, because she feared the anesthetic, but finally agreed to it, with an excellent result. We heard from her a year later, and found that we had freed her from rheumatism and made a most grateful patient besides.

The presence or absence of rheumatic heart disease made no difference when we had once made up our minds that the focus was in the tonsils, and the operation was necessary. In a majority of these cases no demonstrable cardiac involvement could be discovered upon careful physical examination.

In the 13 cases which occurred after operation we would want to ascertain just how the operation was performed and what the condition of the throat was a few weeks after operation. Our examinations showed that enough tonsil was left in a considerable number of cases to make a dangerous focus in people who were supposed to have had the tonsils thoroughly removed.

A physician examining the figures of this report would be unable to see any material difference between the tonsillectomized and the untonsillectomized cases. Like most statistics on this subject gathered from adult subjects, they are unconvincing. To make the operation of value it is our opinion that it should be performed upon children while the foci of infection are still limited to the tonsils.

CONCLUSIONS

1. It is our belief that complete enucleation of the tonsils offers the best preventive of rheumatic fever, and therefore of rheumatic heart disease. That it will prevent every case of rheumatic heart disease is, of course, beyond our expectation.

2. A history of repeated sore throats is of more importance than tonsils which by appearance suggest disease. The British

report, and most observers who have made a careful study of the problem, emphasize this point. Repeated sore throats even with tonsils of normal appearance, call for tonsillectomy.

3. The reverse is equally true—that if the tonsils are diseased in appearance, they should be enucleated even in the absence of sore throat.

4. Physicians should have a thorough understanding of the insidious signs of acute rheumatism in its earliest stages, remembering that the disease has wide differences from that seen in adults.

5. Tonsillectomy is a major operation and should be performed only by persons duly qualified by training and experience.

6. Incomplete tonsillectomies leave the patient in as dangerous a situation as before, and throw discredit upon the value of tonsillectomy as a preventive. Tonsillar remains are often as formidable as the original tonsil.

7. One of the outstanding errors in reasoning seems to be that writers argue that rheumatic heart disease appeared after tonsillectomy had been performed, and therefore tonsillectomy failed as a preventive. It must be remembered that rheumatic heart disease may not declare itself until three or four years after an attack of tonsillitis or rheumatic fever. Furthermore, the mere fact that tonsillectomy was eventually performed indicated the necessity for it—the delay and uncertainty may have made the cardiac damage possible. On the other hand, even a late tonsillectomy will often prevent subsequent attacks and damage to the heart.

8. The prompt subsidence of fever and joint symptoms following tonsillectomy in cases of acute rheumatic fever has greatly encouraged us to resort to the operation as soon as sufficient study has convinced us that the tonsil is the port of entry. Since operation during the height of the febrile attack has not proved disastrous, as some have feared, in our hands, we hope that it will diminish the possibilities of cardiac involvement.

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CLINIC OF DR. FREDERICK T. LORD

MASSACHUSSETTS GENERAL HOSPITAL

A CASE OF SPONTANEOUS SUBDURAL HEMATOMA IN WHICH THE DIAGNOSIS WAS MISSED DURING LIFE

THE following case history is that of a patient who was under observation at the Massachusetts General Hospital from September 24, 1926 to October 11, 1926, when he died. The problem is of sufficient interest and importance to merit publication in the hope that the condition from which he suffered may be more widely recognized and properly treated. A copy of his case history was given at one exercise to each of a group of 47 physicians with the request that a written report of the diagnosis be turned in before the next exercise one week later. Replies were received from 25 of the 47 physicians and are incorporated in this report.

History.—The patient, Mr. R. S. (278917), was forty-three years of age, single, a pattern maker, born in Scotland and living for the past four years in Massachusetts. He has not been well for the past nine weeks.

For the first six weeks of his illness his chief complaint was of inconstant, daily, dull, occipital headache, not more severe to right or left and usually lasting from three to four hours. It was not severe enough to make him groan, but kept him awake and made him very miserable. There was radiation of the headache from the back to the front of the head. There was occasional nausea, but no vomiting. In addition, during this period he was weak and nervous. There was no dizziness, but slight unsteadiness. There was no disturbance of the special senses, or of sensation or motion. He slept thirteen to sixteen hours daily. There was no night urination. There was no cough, dyspnea, or wheezing. The bowels were constipated.

For the last three weeks of his illness he was under observation at the Massachusetts General Hospital and during this time he was increasingly drowsy, unable to fix his attention or give any account of himself. Under observation there was apparently no headache.

Of other matters pertaining to the history, he served in the British Army during the war and was wounded twice, once by a bursting shell with injury to the right side of the face and the right malar bone. Plastic surgery was, in consequence, done on the face. He was also wounded in the heel. A good recovery was made from both injuries. There was no history of any more recent injury. He was a man of good habits, with a negative family history. His only past illness was measles. He denied venereal disease.

Tentative Deductions from the Story.—It is desirable to attempt to make a tentative diagnosis from the history alone before the physical findings and the results of special tests are known, and thus far a disturbance confined to the central nervous system is suggested. This is evidently of a serious nature with headache, nausea, increasing drowsiness and marked mental disturbance the outstanding features. This complex of symptoms is consistent with an increase of intracranial pressure, but as yet we have no evidence as to the nature or site of the disturbance.

Physical Examination at Entrance to Hospital.—At entrance, he was well developed and fairly nourished, rather thin. The pupils were equal, regular in outline and reacted to light and distance. There was no nystagmus. The field of vision was normal by rough tests. Examination of the fundi with the ophthalmoscope was negative. The neck was stiff for forward bending, but other motions were unimpaired. Palpation and auscultation of the skull was negative. Palpation of the right malar bone showed a shallow depression on its external surface over an area about the size of the tip of the little finger. The scars of the plastic operation were hardly visible. There was no sinus tenderness. The tongue was coated. The throat was negative. There was one capped tooth and much dentistry with slight redness and swelling of the gums about certain teeth. The lungs, heart, and

abdomen showed nothing abnormal. There was no evidence of any cranial nerve paralysis. The speech was unaffected, but he was very apathetic, and although he obeyed commands it was impossible to carry on any conversation with him. There was slight ataxia in the right forefinger to nose test and slight Romberg with an unsteady gait, perhaps from weakness. The biceps, triceps, radials, knee-jerks, and Achilles' tendon reflexes were active and equal. The abdominal reflexes were normal. There was no Kernig. Blood-pressure was 120/85.

Other Findings Under Observation.—Under observation, to mention only the positive findings, it was noted that the left was larger than the right pupil and reacted poorly to light and accommodation. There was difficulty with convergence and almost no upward movement of the eye-balls. The right knee-jerk was more active than the left and there was a Babinski and Gordon reflex on the right.

The temperature was normal throughout his stay in the hospital, and although only infrequently taken before entrance was not known to have been elevated during the illness. Under observation the pulse rate was 60 to 70, the respirations about 20. The urine showed nothing abnormal. Examination of the blood showed a red count of 6,080,000, and a white count of 8000 to 10,000. Hemoglobin 65 to 85 per cent. Blood-smear negative. Wassermann test on blood negative. The non-protein nitrogen in the blood amounted to 40 mgm. per 100 c.c. of blood. The normal is about 25 to 35 mgm.

Roentgen-ray examination showed the sinuses to be large. The sella turcica was normal in size and shape. The blood-vessel markings in the film of the skull were unusually prominent. The markings of the convolutions could not be made out.

Deductions from the History and Physical Examination.—Physical examination has given us some additional information. He is evidently suffering from a grave intracranial disturbance. The suspicion from the story that an increased intracranial pressure plays a part in the process is not confirmed by the finding of optic neuritis. It may be noted that the headache so troublesome during the first six weeks was not apparently a

symptom during the last three weeks of the illness. As optic neuritis is not an invariable accompaniment of an increase of pressure within the skull, its absence does not justify the conclusion that there is no increased intracranial pressure. The question of increased intracranial pressure is of practical importance at this period in the discussion because a decision must be made whether or not it is desirable to make an examination of the spinal fluid. The withdrawal of a few cubic centimeters of spinal fluid is not ordinarily dangerous, but may be followed by headache which occurs when the patient sits up and subsides when he lies down. Such headaches are probably due to the continued escape of spinal fluid through the puncture hole in the dura and may persist for a few days to a week or more after the procedure. They are troublesome, as they keep the patient abed, but are not dangerous. In the presence of increased intracranial pressure, however, there is actually some risk of a fatal termination after the withdrawal of spinal fluid, and examination of the eye-grounds for optic neuritis should always be made before lumbar puncture is attempted. In the presence of increased intracranial pressure with cerebral tumor the release of pressure by removal of fluid from below may serve to herniate the base of the brain into the foramen magnum and breathing may in consequence stop from pressure on the respiratory center in the medulla. This is a danger we should have constantly in mind in such cases, and I feel that I should emphasize it, because on one occasion a patient with cerebral tumor on whom I did a lumbar puncture stopped breathing within a few minutes thereafter, and recovered only after the performance of artificial respiration for a period of six hours. Lumbar puncture may also be dangerous shortly after the occurrence of intracranial hemorrhage, and under such circumstances may lead to a recurrence of hemorrhage. In cases in which tumor or recent hemorrhage is suspected, therefore, there should be a resort to this procedure only after due consideration of the possible dangers. In febrile cases with headache, nausea, vomiting, and optic neuritis, and a suspicion that the patient may have meningococcus meningitis, we are justified in taking the slight risk which the removal of

spinal fluid entails in view of the benefit to be expected from the administration of antimeningococcic serum. Syphilis of the central nervous system with blood negative to the Wassermann test is not very infrequent, and the possibility that such a disturbance is the cause of the patient's symptoms justifies the attempt to establish the diagnosis by an examination of the spinal fluid, even at some risk.

With these considerations in mind, should an examination of the spinal fluid be made in this case? Absence of fever and leukocytosis in the face of the unfavorable progress exclude meningococcus meningitis from serious consideration. But syphilis cannot be excluded in spite of the negative Wassermann test on the blood, and on this account and in the hope that even in the absence of syphilis evidence of value may still be obtained, lumbar puncture seems desirable. The absence of optic neuritis gives some assurance that there is no special risk in the procedure.

Results on Examination of the Spinal Fluid.—Lumbar puncture was performed twice without unfavorable consequences. On the first occasion, fifteen days ago, there was no indication of the presence of any pressure in the spinal fluid tested by the manometer. The normal pressure in persons at rest, using a standpipe manometer, is from 70 to 190 mm. If the patient is excited and tense it may be much higher than this. With jugular compression there was slight, if any, increase in the rate of flow. Five to 6 c.c. of blood-tinged fluid was obtained and the flow then stopped. This was xanthochromic and showed a sediment of red cells after centrifuging. The cell count was 12,700, of which 700 were white cells. Differential count showed 76 per cent. polynuclears and 24 per cent. lymphocytes. The normal number of cells in the spinal fluid varies from none to five. Wassermann test of the fluid was negative. The total protein was 100. Normally the protein amounts to from 15 to 45 mgm. per 100 c.c. Sugar 76. The normal sugar is 50 to 75. Culture was negative. Gold sol 111232000. Any figure higher than 1 in the gold sol reading is pathologic.

The lumbar puncture was repeated one week later, and again no pressure was determined with the manometer, but on this

occasion there was definite increase in the rate of flow with jugular compression done bimanually only. The fluid. 5 c.c. in amount, was xanthochromic as before. The red cells numbered 590 and all were crenated. The white count was 20, all lymphocytes. The total protein was 80. Chlorids 720. This is normal. Sugar 80 and gold sol 1111000000.

Cistern puncture, fourteen days ago, showed practically no pressure, and jugular compression was without response. The fluid 3 c.c. in amount, was slightly turbid and xanthochromic. Red cells 297, whites 12. Total protein 50. Sugar 56. Gold sol 0011100000.

With these spinal fluid findings at hand, what conclusions can we draw from them? Under normal conditions a prompt elevation of pressure is to be expected from jugular compression, and its absence suggests the presence of block above the level of the puncture. In this case a block if present must be at or above the level of the foramen magnum. The presence of crenated red cells (erythrochromia) and yellow color (xanthochromia) are abnormal features. The presence of red cells in all three fluids suggests that these cells were contained in the fluid and were not due to the puncture. The yellow color tends to confirm this supposition, and this color may be ascribed to the presence of hemoglobin. The abnormal chemistry of the fluid and the slightly abnormal gold sol may be due to the presence of blood and thus have no other special significance.

It should be noted that red blood-cells were present in the spinal fluid on all of the three occasions. In obtaining spinal fluid for examination it is desirable to collect the specimen in several test-tubes as successive samples in order that evidence may thus be obtained regarding the source of blood which appears in the fluid. Blood due to the puncture may then appear in largest amount in the first tube, while blood present previous to the puncture is likely to be evenly distributed in the various samples. Owing to difficulty in obtaining fluid in this case only one sample was secured at each puncture.

Diagnosis of the Nature of the Disturbance.—We may now attempt to put the complex together and consider the diagnosis

made by the twenty-five physicians who made a report on this problem.

The largest number of votes, seven in all, were cast for the diagnosis of lethargic encephalitis. Headache, mental disturbance, drowsiness, weakness, ocular palsies, and the absence of optic neuritis are common to this disease and the case under discussion. But the spinal fluid in lethargic encephalitis is clear, under normal or increased pressure, and shows a slight increase in cells all of which are lymphocytes. The presence of an intracranial block, numerous red cells, and yellow fluid make lethargic encephalitis very unlikely. Absence of fever and leukocytosis are also against it. Some type of syphilis was the diagnosis in six of the reports. The disease is denied by the patient. There are no syphilitic manifestations outside the nervous system. In syphilis of the central nervous system the spinal fluid is clear under normal pressure and the gold sol is likely to present a characteristic curve. An increase of cells, mostly lymphocytes, is present. Above all, however, a positive Wassermann test is to be expected in both the blood and spinal fluid, and if not in the former at least in the latter in cases of syphilis of sufficient severity to give rise to the grave manifestations presented by this patient. On these grounds it seems to me syphilis can be excluded.

The diagnosis was brain tumor in five of the replies. In its favor are such general symptoms as headache, nausea, increasing drowsiness, and severe mental disturbance. Absence of fever and leukocytosis are consistent with this explanation. The absence of optic neuritis cannot be said to be against it. The progress from bad to worse is especially suggestive of tumor. Localizing signs have more recently become a part of the picture and suggest that if present a growth is rapidly extending, or that there has been a hemorrhage in or about it. Partial or complete block at or above the level of the foramen magnum may be due to a developing tumor. Red blood-cells in the spinal fluid and its yellow color are out of accord with this explanation of his symptoms, and necessitate the assumption that if tumor is the cause it is complicated by hemorrhage. Tumor with hemorrhage cannot be excluded.

Intracranial hemorrhage is suggested by two of the replies. In the absence of a history of injury more recent than that from the bursting shell during the war it is reasonable to regard as unlikely such types of intracranial hemorrhage as are commonly the result of trauma. The chronic and unfavorably progressive course is consistent, however, with the chronic type of subdural hemorrhage; but the localizing signs are not suggestive of the usual site of such a hemorrhage in the parietal region. Inasmuch as there are indications of intracranial disturbance, and the spinal fluid findings are consistent with the escape of blood into the intracranial cavity and thence into the spinal canal, the diagnosis of intracranial hemorrhage may be regarded as established.

Cerebellar abscess, brain abscess, cerebrospinal meningitis, cerebral thrombosis, or myelitis was the diagnosis in the five remaining replies. The first three of these explanations may be dismissed as unlikely from the absence of indications that the disturbance is of inflammatory nature. At his age cerebral thrombosis is most commonly the result of syphilitic arteritis. Syphilis seems to be adequately excluded, but the possibility of an arteritis due to another cause cannot be denied. The history of headache is against it and it need not be seriously considered. The term "myelitis" implies an inflammation of the spinal cord, and of this there is no evidence.

Location of the Disturbance.—Of the five replies with a diagnosis of tumor, the location was not stated by one. The tumor was regarded as in the cerebellum by two, and in the pons and left motor area in one each. One of the two who ascribe the disturbance to intracranial hemorrhage thought the site of the bleeding the cerebral region, the other the region of the corpora quadrigemina or the cerebellum.

The data which can be used in the attempt to localize the lesion are meager and confusing. Granting that the site of pain is an uncertain indication of the location of the process, yet the constant complaint of headache referred to in the occipital region may be taken into consideration. The presence of a disturbance of equilibrium and ataxia suggest involvement of the cerebellum

and to some extent support the supposition that the occipital region may be the site of the disturbance. Apathy and blunting of the mental faculties, on the other hand, bring the frontal lobes into the picture. The most suggestive focalizing signs are the dilatation and rigidity of the left pupil in combination with the exaggerated right knee-jerk and the right Babinski. Involvement of the left crus is the most likely explanation of this combination. The disturbance of convergence and of upward movement of the eyes suggests involvement of the region of the corpora quadrigemina and the posterior longitudinal bundle.

Conclusions Regarding the Diagnosis.—Intracranial hemorrhage may be regarded as established. Cerebral tumor complicated by hemorrhages is also a possibility. The focalizing signs point more particularly to a lesion in the midbrain, and if this is the site it is inaccessible to surgery.

Findings at Autopsy.—Postmortem examination was made by Dr. Tracy B. Mallory. On removal of the calvarium the dura was seen to bulge slightly over the parietal and frontal regions on each side. On palpation these areas fluctuated markedly. Removal of the dura showed a diffuse area of hemorrhage on its inferior surface over both hemispheres. On the left the hematoma measured 14 x 8 x 2 cm., on the right, 12 x 7 x 1 cm. The blood was chiefly clotted, but a portion of it was still fluid. Along the borders the clot was somewhat grayish, friable, and fairly firmly adherent to the dura. The inferior surface of the clotted areas showed a distinct thin membrane which separated it from the pia-arachnoid. The vessels of the pia were deeply congested and somewhat dilated, but otherwise negative. The vessels of the circle of Willis were negative. The sinuses showed nothing abnormal.

The brain showed a distinct depression over the left frontal and the left parietal areas with a narrow bridge of depressed tissue between. There was slight, if any, depression of the right. These depressions correspond with points of greater thickening of the subdural hemorrhage. The brain tissue was firm. The ventricles were somewhat collapsed and contained very little fluid. This was slightly cloudy, but showed no fresh blood. The

choroid plexus was apparently normal and the ventricles communicated freely with each other. Careful sectioning of the midbrain region revealed no pathology.

On microscopic examination, the choroid plexus showed thrombosis of several of the smaller arteries. The membrane separating dura and clot is composed of fairly old, well-formed fibroblasts, between which are numerous large capillaries lined with endothelium. Very few of them are blood filled, none contain fibrin or granular débris. No mesothelial-lined spaces are observed. In a few areas there is a suggestion that the membrane is composed of two layers of different ages. The separation of membrane and clot is very sharp and there appears to be no organization spreading from the membrane into the clot, although on the inferior surface an organizing process is spreading up rapidly from the neomembrane. The latter is composed of fibrous tissue without distinctive character. The picture is characteristic of the "spontaneous" type of chronic subdural hematoma rather than the "traumatic" variety, as the two are classified by Putnam and Cushing.[1]

The clinical diagnosis of intracranial hemorrhage was confirmed at autopsy. No tumor was found. The site of the lesion was not in the midbrain, but under the dura overlying the parietal and frontal lobes on each side. If the evidence had indicated that he had hemorrhage in a region as easily explored with the trephine as the subdural space overlying the parietal and frontal lobes, its discovery by this means might have been the means of saving his life.

Explanation of the Clinical Picture.—With the autopsy findings it is possible to explain the clinical picture. The war injury is probably unrelated to the condition. The latent interval between trauma and onset of symptoms in patients with subdural hemorrhage is usually less than a week, and in over 80 per cent. of the cases less than three weeks, but may extend over a period of months. In the case reported by Buss[2] two years elapsed between a severe fall and the onset of symptoms. In

[1] Archives of Surgery, 11, 1925.
[2] Zeit. f. klin. Med., 38, 451, 1199.

one of Putnam and Cushing's cases there was a period of two years between a head injury and manifestations ascribed to hemorrhage.

The evolution of the symptoms is significant. The headache was due to increased intracranial pressure and stretching of the brain membranes. During the first six weeks of the illness the increased pressure was not sufficient to cause any considerable interference with function, but as the amount of blood increased there was sufficient pressure on the frontal lobes to cause apathy and mental incapacity. As encroachment on intracranial space increased there was transmitted pressure on the midbrain and its neighborhood with consequent localizing signs referred to one crus, the corpora quadrigeminal region and the cerebellum. No block was found at autopsy, but it is probable that crowding of the structures at the base of the brain into the foramen magnum interfered with the free transmission of pressure from the intracranial to the spinal fluid.

CLINIC OF DR. CYRUS C. STURGIS

THE PETER BENT BRIGHAM HOSPITAL

ORGANIC LESIONS IN NEUROTIC PATIENTS

IT is of great interest to speculate about which type of error has been the source of greatest evil; the failure to recognize an organic disease in a neurotic patient or the radical treatment, such as surgery, of a non-existent organic condition in a patient whose complaints rest entirely on a neurotic basis. Undoubtedly both types of diagnostic errors are in some instances unavoidable, as many times the thoughtful and careful clinician is sorely tried when confronted with either one of the above possibilities. A certain quota of mistakes, however, result from faulty and superficial methods of study which are inexcusable. I have selected the records of 3 patients with duodenal ulcer to present, not that I wish to discuss especially the diagnosis of this condition, but rather because the case histories of these patients are examples of the failure to recognize an organic condition, as the patients presented all of the obvious earmarks of neurotic individuals. That the discussion centers about 3 patients who were suffering from duodenal ulcer is unimportant, as the point might be illustrated adequately by any organic disease which does not show striking objective signs on the ordinary physical examination. Examples of such diseases which may fall into this group are angina pectoris, cholelithiasis, pulmonary tuberculosis, and many others.

There can be no better illustration of the value of considering the patient as a whole than the situation which is presented by a neurotic patient with an organic disease. Consider the instance of a supposedly healthy man of middle age who suddenly develops symptoms referable to the heart which, for example,

might indicate angina pectoris. It is entirely possible that the physical examination in this disease might show no abnormal signs, and the correct diagnosis, therefore, must be deduced entirely from the patient's history. If for some inherent reason the patient's emotional reaction is greatly exaggerated, it might result that a most profound neurotic syndrome is superimposed upon and completely masks the underlying cardiac condition. Why one patient will be completely upset with worry and apprehension concerning a symptom, and another will have slight if any emotional reaction, depends upon many factors. Certainly heredity plays a fundamental rôle, and often other things, such as environment, are of importance. It frequently occurs that a patient will develop an abnormal fear of a fatal disease through close contact with it in a friend or relative, and all of the characteristic symptoms of a neurosis, therefore, are added to those which have an organic condition as their basis.

It sometimes occurs that a physician, having once accomplished a striking cure of a neurotic individual by proper management, may become too enthusiastic and forget that a patient may be suffering from a severe organic condition and, in addition, have a pronounced but unrelated neurosis. The entire subject of functional mental condition is of vast importance to the practitioner, and, although it deserves careful attention, it is probable that patients with this disorder are less efficiently managed than any other group encountered in medicine. Among other reasons this is doubtless due to the failure of a great many medical schools to teach this variety of medicine adequately, and, what is more regretable, some physicians, through lack of interest or time, neglect such patients. The past ten or fifteen years, however, has seen much improvement in these conditions, as the present-day practitioner more clearly understands functional mental disorders and appreciates the great amount of good which can be accomplished by the proper therapy.

In order to illustrate various points I wish to discuss the clinical histories of 3 patients with duodenal ulcer, as the correct diagnosis of this disease is based chiefly upon the information given by the patient, unless Roentgen-ray studies are

made. If hematemesis or tarry stools have occurred, which happens in a minority of these patients, the diagnosis is at once suggested; but it is interesting to note that such a striking phenomenon as this should be forgotten as it was by one of the patients herein reported who failed to give this information in reply to a direct question, and finally recalled that he had previously observed this phenomenon, when his attention was called to a stool of this type which he had defecated while in the hospital. The other cardinal symptom of duodenal ulcer is pain or epigastric distress, and when this occurs characteristically in relation to food, and, in addition, the patient states that relief follows the ingestion of alkalies, the diagnosis is usually clear. In fact, if sufficient time is permitted to study such patients, there are few diagnoses which can be made with the same degree of accuracy from the history alone. The greatest number of errors result from the inability of the patient to give an accurate history, or, because of the coexistence of either a related or unrelated neurotic tendency, the symptoms due to the latter condition completely dominate the picture. Thus it sometimes follows that the patient is not selected to undergo Roentgen-ray studies of the gastro-intestinal tract and the true condition is not recognized. The solution of the diagnostic difficulties presented by such patients lies in (1) more careful histories in patients with organic diseases which do not ordinarily produce objective signs on the usual routine physical examination, and (2) a longer period of observation and more wide-spread employment of special methods of study, such as the Roentgen ray, before a final diagnosis of a purely functional mental condition is deduced. The latter may lead to a large number of Roentgen-ray studies which show no abnormalities, but nevertheless this would reduce the number of erroneous diagnoses.

Case I.—A business man, age fifty-four, was admitted to The Peter Bent Brigham Hospital on March 8, 1926, with the chief complaint of "belching gas." The patient had always been strong and healthy until the onset of his gastric symptoms about ten or twelve years before. Since then he had suffered from at-

3180

tacks which developed three or four times a year and persisted for four to eight weeks. At these times he experienced rather sharp, distressing pain all over the abdomen which began in the lower quadrants and extended upward. The pain was not accompanied by diarrhea or constipation. It was relieved by belching and passing gas per rectum. He frequently vomited a rather large amount of watery material, usually between 5 and 8 P. M., or around midnight, which gave him relief. Food likewise diminished the pain and soda was of some assistance, as it induced vomiting. Two years ago an exploratory laparotomy was performed on account of these complaints, but nothing of importance was found. The patient had been introspective and worried about his condition. His physician had noted that there was a marked neurotic element associated with his complaints, as hypodermic injections of sterile water had frequently given him relief. Moreover, if his attention was diverted from his symptoms by any means, they usually ceased for a brief interval. The attack which brought him to the hospital had been of four weeks' duration. His symptoms, though becoming worse, did not differ essentially from those previously experienced. Physical examination showed a somewhat undernourished, middle-aged man who was emotionally unstable, as he wept when discussing his difficulties. Otherwise the examination showed no abnormalities.

While this patient's history is highly suggestive of duodenal ulcer, his physician was diverted from the true diagnosis on account of the obvious neurotic demeanor of the patient. Why his pain should be relieved by a placebo is not understood, but nevertheless it has been known to occur in other similar cases, and may be responsible for an erroneous diagnosis.[1]

Roentgen-ray studies of the gastro-intestinal tract showed that there was a six-hour residue, estimated at 10 per cent., in the stomach. The duodenal cap was small, constantly irregular,

[1] Another patient, with whom I was familiar, passed through the hands of many physicians, all of whom considered that he was neurotic because his epigastric distress disappeared when he indulged in his favorite pastime of playing cards. He was subsequently found to have an ulcer in aberrant gastric mucosa which was located in the lower end of the esophagus.

and presented a small crater on the lesser curvature side. There was definite tenderness over this area. The findings were highly characteristic of a duodenal ulcer.

The further course of this patient is interesting from the standpoint of the reliability of a medical history. While still under observation he developed evidence of bleeding from the gastro-intestinal tract as indicated by faintness, tachycardia, profuse, perspiration, and tarry stools. Although he had previously denied such symptoms, he recalled following this attack that he had experienced the same symptoms before and had observed a similar type of tarry stool. He was apparently so intense about his present symptoms that a point was overlooked in his history which was of great importance, although of course he did not appreciate the relationship between a stool of this character and his abdominal complaints.

What are the important points for consideration in this patient? In the first place the most striking feature, superficially, was his nervousness. This was the first condition which any person, physician or layman, would note. He was apprehensive about his health, introspective, discouraged, and was so unstable as to lose control of his emotions and weep. Confirming this first impression of the patient was the statement, which was unquestionably true, that his most striking symptom, pain, was relieved by a placebo, or by diverting his attentions to other subjects. Surely a history such as this would influence many physicians to consider that a neurosis was responsible for most of his complaints.

What was there against such a diagnosis? Careful analysis shows that there was a great deal. This patient had no underlying cause for a neurosis as far as could be determined. He was a successful business man, a respected member of his community, happily married, with no worries, financial or otherwise. This information was reasonably certain, and it therefore appeared that his only source of anxiety was abdominal distress, which had persisted for a long time without permanent relief. His mental reaction to this situation cannot be considered abnormal. It is also important to note that this patient was fifty-four years

of age. This fact alone makes the diagnosis of a pure neurosis more difficult, not because these conditions have a tendency to become less at this age, but because as a person approaches middle life the incidence of chronic disease increases. Malignancy, especially if the patient has a gastric complaint, must receive careful consideration. Likewise at this period of life other diseases, such as angina pectoris, the late manifestation of syphilis, and arteriosclerotic changes, must be kept in mind. These two facts alone, the patient's age and the lack of etiology for a neurosis, should have cautioned against such a diagnosis. Another fact against it was that the patient had never shown evidence of a neurotic tendency until the onset of the present illness. While it undoubtedly occurs, nevertheless it would be unusual for an individual to develop symptoms of a purely functional nervous disorder for the first time at the age of fifty-four. In most instances some evidence of this tendency appears at a much earlier age.

A consideration of the patient's history from the standpoint of an organic disease of the gastro-intestinal tract shows clean-cut evidence of a peptic ulcer, when these symptoms of this condition are sifted from the neurotic complaints. The characteristic points were as follows:

1. Long-standing (ten to twelve years) abdominal distress which appeared in attacks of four to eight weeks' duration on the average of two to three times a year.

2. The most intense distress appeared between 5 and 6 P. M. and about midnight. It was relieved by vomiting, soda, belching, or the ingestion of food.

These two statements alone should strongly suggest the diagnosis of gastric or duodenal ulcer. In addition, examination of a specimen of fasting gastric contents showed corroborative evidence, as follows: Volume 125 c.c.; yellow, watery, microscopic negative. Free HCl 69 acidity per cent., combined HCl 8 acidity per cent. The benzidine test for occult blood was strongly positive. This evidence, when combined with the history, made the diagnosis of ulcer highly probable, and final confirmation was obtained by gastro-intestinal Roentgen-ray studies.

Case II.—Male, age fifty-one, who complained of "distress in the stomach." He had always enjoyed good health up until the onset of the present illness. His occupation was that of foreman in a small factory of which he was part owner. The business, which had previously been prosperous, had recently declined to such a point that it was necessary to reduce the patient's already inadequate salary. He considered that this was fair under the circumstances and, in addition, said that he had no recourse, as he could not obtain another position or learn a new trade at his age. He felt his lack of success keenly and deplored the fact that when he should be enjoying the fruits of an honest life and hard labor, he was in a position wherein he could not even support his family.

Present Illness.—The patient volunteered the information that beginning one year before admission to the hospital he had developed attacks of epigastric distress which were associated with distention of the "stomach" and relieved by belching or passing gas per rectum. He admitted that he was worried and apprehensive about his physical condition as well as his financial embarrassment and his disappointment in life. Had not persistent questioning been carried out, the history would have consisted of vague and unrelated complaints. For the present let us consider that this constitutes the story of the present illness, for this was the only data which was readily obtainable.

The physical examination showed a somewhat apathetic individual who was well developed and nourished and in whom no abnormalities were observed further than the neurotic turn of mind. That the patient was neurotic cannot be doubted. He has suffered misfortune and at the time he came under observation his mental attitude was one of dismal failure without enough energy or ambition to combat his obstacles. In addition, he appeared to be healthy and was well nourished. There might easily be a tendency to attribute all of his symptoms to a purely functional type of gastro-intestinal disorder. Further information was obtained by painstaking and patient questioning. The attacks of abdominal distress, which he localized in the upper part of the abdomen, appeared at any time of the day or night,

but apparently there was a tendency for it to occur two or three hours after meals. The distress was relieved by soda and in part by food. His symptoms were not constant, but appeared for a period of a week or ten days and then disappeared for three or four weeks. His appetite had been very good and there had been no loss of weight. This additional information, of course, suggested very clearly that the patient had a duodenal or gastric ulcer, but at the time it was obtained the appraisal of its value was a different task. Gastro-intestinal Roentgen-ray studies showed very definitely an ulcer of the duodenum with spasm and hyperperistalsis of the stomach. Operation confirmed these findings.

Case III.—A male, age thirty-four, policeman, complained of "indigestion with recent vomiting and backache."

Past History.—The patient admitted that he had always had a very nervous temperament and had experienced fainting attacks. During his wife's second pregnancy he stated that he was greatly upset and worried and frequently vomited in the morning, but otherwise had no gastro-intestinal complaints.

Present Illness.—After twenty-two months' service in France the patient returned home in 1919. At this time he complained of "gas and indigestion," but was not troubled with abdominal pain. The attacks did not have a definite relation to meals and the only thing which gave him relief was beer. He usually experienced these symptoms for a period of three or four weeks, after which there was a remission of all complaints for approximately an equal period of time.

Physical examination showed a somewhat undernourished man with an obviously nervous and overalert demeanor. There was slight and apparently insignificant tenderness on deep pressure in the right lower quadrant of the abdomen. Otherwise the physical examination was negative. The physician who examined this patient was pressed for time and did not secure a complete history, as it was exceedingly difficult to obtain accurate data from the patient. Although the patient was regarded as highly neurotic, good judgment was exercised, and gastro-in-

testinal studies were obtained which disclosed a definite duodenal ulcer. The patient's symptoms promptly disappeared following the use of the Sippy diet. It is doubtless true that a fairly clean-cut and characteristic history of a duodenal ulcer should have been obtained by persistent and tactful questioning, provided the physician who secured the history had a clear understanding of the symptoms of this condition, and sufficient time was available. The one impression which the examiner did obtain was that the patient had neurotic tendencies, but this was obvious and, in addition, misleading, for attention was diverted from the underlying condition which was the cause of the patient's complaints.

The following case history is given in order to contrast the symptoms and physical findings with those of the preceding patients:

Case IV.—The patient was a married woman, sixty years of age, whose chief complaints were "abdominal distention with belching of gas."

Family History.—The patient's father and mother were both of an irritable, nervous type. She had had twelve children, eight of whom are living and well.

Past History.—There was no history of important illness except the condition related in the present illness.

Present Illness.—Four or five years before admission the patient developed attacks characterized by "queer sensations" in the region of the epigastrium. These were of a rather mild nature, unrelated to the ingestion of food, and relieved by the eructation of gas. The patient had observed this method of obtaining relief and, therefore, resorted to it frequently throughout the day and night. The belching was often so prolonged and audible that it made her conspicuous, and for this reason she declined to appear in public. The patient's appetite was good and there had been no loss of weight.

Before considering this patient's history further let us discuss the situation as given above, which was the only information which the patient volunteered. The striking eructation of gas

suggested, as it always should, that this was accomplished by swallowing air and then belching it up. It was, therefore, considered that at least one of her chief complaints was probably of a functional character. In accord with this was her statement that both her father and mother were of the irritable and nervous type. Her heritage, therefore, indicated a neurotic background, which is often the case in patients with functional gastric conditions. There were no symptoms or signs suggesting peptic ulcer or cancer of the stomach. Her appetite was good, there had been no loss of weight, and she gave the appearance of health. Her examination thus far suggested the typical syndrome of a functional gastric condition, but nevertheless gastro-intestinal Roentgen-ray studies were advised in order to eliminate any organic condition. During this examination only one important thing was observed—the patient was seen to swallow air and regurgitate it. With this information in hand the following additional history pertaining to her psychic life was obtained:

The patient had always had a tendency to be irritable and easily upset nervously. She had raised a large family and worked hard which had prevented her from making social contacts and enjoying suitable diversion. There had been a difficult family situation for years which had been the source of a great deal of worry and disappointment to the patient. This was due to the fact that her husband and only son drank to excess and often humiliated her by their appearance in public when intoxicated. She had met this situation perfectly well until the onset of the present illness four or five years ago, at which time she became depressed and morbid over her difficulties. At the onset her family showed solicitude and sympathy toward her complaints, but when they became chronic their attitude had changed and they no longer showed the same interest. As a result she had "lost heart" and saw no hope of escaping a situation which had become intolerable to her.

After a thorough study of the patient had been completed and all organic conditions eliminated, as far as this was possible, she was assured that no anatomic defect was observed. The mechanism of belching was explained and the relation of her

condition to the family situation was discussed, and arrangements were made to correct this. After a reasonable period of rest and diversion the patient made a complete recovery. The diagnosis of functional gastric condition seemed reasonably certain.

It was not difficult to picture the confusion which might result and the great possibility of a diagnostic error if this patient had suffered, in addition to the purely functional condition, from cholelithiasis which had not produced attacks of typical gall-stone colic. It would have been impossible to separate and appraise correctly the vague symptoms of her disorder from those of a purely neurotic character even though it had been suggested that gall-stones were responsible for some of the patient's symptoms. Moreover, when a patient presents the typical neurotic picture, it not infrequently happens that a physician is inclined to minimize and, therefore, disregard other evidence which suggests the coexistence of an organic disease.

If such a confusion of data exists, and it is not uncommon to encounter just such a situation, the diagnosis of a functional condition, despite the characteristic history, should be deduced chiefly by exclusion. This means that every known clinical test of value should be applied and the final conclusion drawn from it. Very often the correct diagnosis is recognized only after a period of observation. For during this interval the appropriate treatment of a functional condition may produce striking results, or the patient may experience an acute attack, gall-stone colic, for example, which completely dispels all doubt concerning the diagnosis. It is regretable that this type of patient becomes dissatisfied and drifts from one physician to another before a careful and prolonged study can be completed, and as a result there is often a delay in recognizing the true character of the patient's disease.

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ACUTE INFECTIONS OF THE NASOPHARYNX AND ITS ADNEXA IN INFANCY AND EARLY CHILDHOOD

ACUTE nasopharyngitis is probably the most common disease of infancy and early childhood. It is usually looked upon as a trivial matter not only by the laity but also by most physicians. In infancy, however, it may of itself be fatal, while in childhood it is not infrequently the cause of death through its complications. Every case of nasopharyngitis, no matter how mild, should therefore be looked upon as potentially dangerous and treated accordingly.

Anatomy.—In order to understand why acute nasopharyngitis may be such a serious disease in early life, why complications are so common at this age and why they differ at different periods, it is necessary to know something of the anatomy of the nasopharynx and its adnexa in infancy and childhood, and of the changes which take place in it from year to year.

The nose in infancy is relatively small and the respiratory portion very small. The height of the posterior nares at birth is from 6 to 7 mm. and the breadth between the pterygoid processes at the hard palate 9 mm. The nasal cavity at birth is relatively long and the respiratory portion is very narrow. The whole opening of the posterior nares on either side is just large enough to admit the end of a medium size, male catheter. The nasal cavity begins to increase in height directly after birth, increasing quite rapidly during the first six months, but very slowly during the rest of infancy. The size of the posterior opening doubles in six months, after which it remains stationary until

the end of the second year. The nasal cavity begins to approach the adult shape at the end of the seventh month, although it is still relatively broad. The nasopharynx is very low at birth, but is relatively long from before backward. The height of the nasopharynx increases synchronously with that of the posterior nares. The Eustachian tube is nearly horizontal at birth and opens at the level of the hard palate. It is not only relatively but absolutely wider at its narrowest point at birth and during infancy than it is in the adult. The connective tissue between the nasopharynx and spine is very lax. The nasopharynx is extremely vascular and there is an abundant supply of lymphatic glands and vessels, especially in the posterior wall. The anatomic relations in the nose and nasopharynx gradually change with age, so that by the time the child is seven years old the relations are essentially the same as in the adult.

The ethmoid area is present at birth, but the development into distinct cells does not usually begin until the fourth year, and their development is not well marked until some years later. Nevertheless, infection in the ethmoid region is not at all uncommon in infancy and early childhood in the course of nasopharyngitis.

The frontal sinuses are sometimes present as early as the fifth year, but usually do not amount to much before the seventh or eighth year. They do not have to be taken into consideration, therefore, before middle childhood, and even then they are not likely to become seriously involved.

The maxillary antra are present at birth, but are very small, triangular in shape, and somewhat flattened. They do not change much in shape or increase very much in size until the second dentition. Although small, they may become infected at any age.

The mastoid process is small at birth, as is also the antrum, which is about the size of a pea. The mastoid cells are not present at birth, but develop during infancy, being numerous and of fair size at three years. The rate at which they develop is so variable, however, that it is never safe to assume that even a young infant has no mastoid cells.

Adenoids play a very important part in the etiology of recurrent attacks of acute nasopharyngitis throughout infancy and childhood and, especially in infancy, increase markedly the frequency of complications in the middle ear. It must not be forgotten that adenoids large enough to cause obstruction to nasal respiration are not infrequently present at birth. Chronic snuffles in infancy are most often due to adenoids. Persistence of the symptoms after the acute stage of nasopharyngitis has passed is usually due to adenoids, both in infancy and childhood. Recurrence of attacks of acute nasopharyngitis is most often the result of persistence of the infecting organism in adenoids. A marked tendency to extension to the middle ears in acute nasopharyngitis is also strong evidence of the presence of adenoids. It must never be forgotten in such instances that a small amount of adenoids about the opening of the Eustachian tubes may be the cause of otitis media, although it is not sufficient to produce any symptoms of nasal obstruction. This is true in both infancy and childhood.

Adenoids should be removed even in early infancy, if they cause any symptoms of obstruction to nasal respiration. No infant is too young to have its adenoids removed if they are causing obstruction. It is true that they will probably grow again. Until they do, however, the symptoms which they cause are relieved, and they can be removed again later, if necessary. Adenoids should be removed in infancy whenever there is chronic snuffles not due to syphilis, nasal diphtheria, feeble-mindedness, or some other definite cause. Adenoids should be removed in both infancy and childhood, even if small, if there are repeated attacks of acute nasopharyngitis, in order to get rid of the most common focus of infection. Adenoids should also be removed, whether or not they are associated with nasal obstruction, chronic snuffles or repeated colds, and whether they are small or large, if acute nasopharyngitis is complicated by otitis media. If adenoids are removed as a prophylactic measure in both infancy and childhood on these indications, acute nasopharyngitis will be less common and, when it occurs, will be less frequently accompanied by inflammation of the middle ears. If there are

repeated attacks of acute nasopharyngitis after the adenoids have been removed and the tonsils have ever been affected, they should be removed, as the focus of infection is probably located in them.

Acute Nasopharyngitis.—*Symptomatology.*—Acute nasopharyngitis, or a "cold in the head," is usually simply a disagreeable incident in middle and late childhood, as it is in adult life. Its symptomatology needs no description. In infancy and early childhood, however, owing to the anatomic peculiarities already described, the symptoms are more marked and complications are more common. In infancy acute nasopharyngitis may be a serious and sometimes a fatal disease. A comparatively slight swelling of the nasal mucous membrane in infancy blocks the nose and prevents nasal respiration. This necessitates breathing through the mouth, which the young infant cannot do satisfactorily, especially when asleep. Sleep is so interrupted on this account that its strength is very rapidly impaired. The occlusion of the nose also prevents proper sucking and interferes with swallowing. In consequence, the baby takes but little food, even if hungry, and loses weight rapidly. The loss of weight and strength, as the result of the lack of fresh air, food and sleep, may, in feeble babies, cause death.

Complications.—Otitis media is a very common complication of nasopharyngitis in infancy because of the anatomic peculiarities of the nasopharynx. With the change in these anatomic peculiarities with growth, the frequency of otitis media as a complication gradually diminishes, so that, when the child is seven years old it is no greater than in the adult. Extension to the ethmoid tract is also very common in infancy and early childhood. Its frequency gradually diminishes after infancy throughout early childhood. Ethmoiditis, next to adenoids, is probably the most common cause of the long persistence of colds in babies. The maxillary antra are probably also frequently involved in both infancy and childhood, but, on account of their small size, there are usually no recognizable symptoms of this involvement and the involvement is comparatively unimportant. Chronic inflammation may result, however, in early as in adult

life. Inflammation of the frontal sinuses does not occur, because they are not present, except in rare instances, in infancy, and are still very small during early childhood. Extension of the inflammation downward to the larynx and bronchi may occur at any age, but the tendency to extension is more marked in infancy and early childhood than later—the younger the patient, the greater being the tendency. Cervical adenitis is a not infrequent complication of acute nasopharyngitis, both in infancy and childhood. Retropharyngeal abscess is an occasional complication in infancy, but seldom occurs after three years. Endocarditis and nephritis are very rare complications in infancy and occur more frequently in early childhood. The most important point, however, to be remembered about the complications of acute nasopharyngitis in infancy and early childhood is that, if the individual does not have acute nasopharyngitis, it will not have any of the complications and will not be exposed to any of the dangers which these complications carry with them.

Treatment: Preventive.—The most important part of the treatment of acute nasopharyngitis is the preventive. The operative treatment has already been taken up. No preventive treatment can be successful unless the etiology of the disease in question is known. Acute nasopharyngitis is unquestionably due primarily to micro-organisms. As regards the preventive treatment, except by vaccines, it makes no difference what these micro-organisms are, whether staphylococci, streptococci, the Diplococcus catarrhalis, or some as yet unknown specific organism. The important thing is to prevent exposure to an infection by these organisms. This can only be done by the separation of adults and older children with colds in the head from babies and young children until they are well. Older children and adults, when they have colds, must not be allowed to come near babies and young children. Children with colds can be isolated, although it is difficult to isolate adults. If it is impossible in any other way, well babies and young children should be isolated so that others cannot come near them.

In most instances, however, there seems to be another element besides direct exposure to contagion in the etiology of acute nasopharyngitis. This must be the chief element in those instances in which there is no apparent exposure, the infection being presumably by micro-organisms already present in the nasopharynx of the individual, but unable to gain a foothold under normal conditions. The mucous membrane of many children is undoubtedly more than normally vulnerable. This vulnerability is sometimes, perhaps, the result of heredity, but is more often due to the mode of life, which lessens the resistance of the mucous membrane to infection. Overheated houses, dryness of the air, and lack of fresh outdoor air unquestionably predispose to infection. An excess of clothing, which causes excessive perspiration, makes it easy for children to get chilled. An insufficiency of clothing also predisposes to chilling and infection. Wetting the feet, sitting in drafts, exposure to cold and wind, especially if it is dusty, are so often followed by a cold in the head that it is evident there must be some connection. It is probable that the connection is that these things change the blood-supply of the nasal mucous membrane or irritate this membrane so that its resistance to infection with micro-organisms is temporarily diminished.

A very important part of the preventive treatment of acute nasopharyngitis is, therefore, regulation of the daily life of the child. It should live in a house kept at an even temperature, neither too hot nor too cold. From 68° to 70° F. is probably the optimum. Lower temperatures are better than higher. The air of the house should be kept moist. Both babies and children should have fresh air both by day and at night. Exposure to the night air does not cause colds in the head. If children have a vulnerable mucous membrane, they should be kept in the house on windy and dusty days, but should have the windows open part of the time. The clothing must be regulated to the temperature of the house in which the child lives. If the house is hot, the child should wear thin clothes while indoors and put on thick clothes when it goes out. If the house in which it lives is cold, it should wear thick clothes indoors and does not

need to put on many extra wraps when it goes out-of-doors. The two points to be remembered are that the child must not have on so many clothes that it perspires whenever it exercises and that it must have clothes enough on so that it does not get chilled.

Bed.—A young baby will, of course, be in bed anyway when it starts in with a cold in the head. An older baby or young child should be put to bed at once and kept there for two or three days. It may seem unnecessary to put a child with a cold in the head to bed. It may be in many instances. Nevertheless, in almost every instance time is saved by putting a child to bed, and it will lose less fresh air and time than it will if it is allowed to be up and about. The acute stage is shortened and complications are avoided. Other children should be kept away from the patient. The temperature of the room should be about 64° F. If the child is not put to bed, it should certainly be kept in the house. Under no circumstances should a child with a cold in the head be allowed to go to school. If it is up, the temperature of the room should be between 68° and 70° F. It goes without saying that the air of the room should be changed and kept pure.

Diet.—There are no specific indications as to the diet in acute nasopharyngitis. A baby that is on the breast should be kept on the breast. If it is unable to nurse, the milk should be drawn and fed to it. If it is on the bottle, it is wise to dilute the food a little. The diet of young children should be regulated largely by the temperature. If they have no fever, it is safe to feed them as usual. If they have a fever, the diet should be somewhat restricted. It is wiser to err on the side of overfeeding than of underfeeding.

Cathartics.—It is useless to give a cathartic to a child after acute nasopharyngitis has developed. It is then too late to diminish the congestion of the nasal mucous membrane by drawing blood to the intestines. It is doubtful, moreover, whether this can be done anyway. A cathartic will probably do no good, therefore, even if it is given when it is suspected that a child is coming down with a cold. Cathartics certainly

cannot diminish the number of micro-organisms which have invaded the nasal mucosa.

Drugs.—There are no drugs which have any curative action in acute nasopharyngitis. There are, however, a number of them which tend to dry up the secretions. Among them are belladonna, atropin, and camphor. They may make the patient more comfortable. On the other hand, many adults feel that the results of the remedy are worse than the disease. It is probable that the action is the same in infancy and childhood. Many of the symptoms, such as malaise and general aches and pains, may, however, be relieved by such drugs as aspirin and phenacetin.

Vaccines, even if autogenous, are not only useless, but are contraindicated in acute infections like nasopharyngitis. They can do no good and may do harm. Furthermore, by the time an autogenous vaccine can be prepared, the acute stage is passed. In cases, however, in which there are repeated attacks of acute nasopharyngitis, apparently not due to contagion, autogenous vaccines may sometimes diminish the number of attacks. A far better method of treatment, however, is to remove the focus of infection.

Local treatment is probably of more benefit, although it is usually difficult to know, when improvement takes place in the course of two or three days, whether it is due to the local measures which have been used or to the natural course of the disease. The silver salts are probably the most useful. It is important not to use too strong solutions. A 5 per cent. aqueous solution of argyrol or neosilvol is strong enough. The silver salts should not be used more than two or three days, because, if they are used longer, they keep up an irritation of the mucous membrane. Liquid albolene may be used freely whenever the nares are occluded. Solutions of epinephrin, in strengths varying from 1 : 1000 to 1 : 5000, may be used alone or in combination with the silver salts. The oily preparations are preferable, because they stay longer on the mucous membrane. After the first few days oily mixtures containing camphor, menthol, and iodin in various proportions may be used. For babies such prepara-

tions should not contain more than $\frac{1}{8}$ grain of iodin, and $\frac{1}{4}$ grain of camphor and menthol, to the ounce. These strengths may be doubled for children.

The only way in which local applications can be made to the mucous membrane of the nose and nasopharynx of babies is by putting the solution into the nose with a medicine dropper while the baby is lying on its back, and letting it run backward into the nasopharynx. This is also the best method to use with young children. As children grow older sprays may be used. Douches should never be used and the nose should never be vigorously sprayed, because of the danger inherent to these measures of setting up inflammation in the middle ear.

A vessel of boiling water in the room, to which compound tincture of benzoin is added from time to time, will often do more to make the patient comfortable than any of these local applications. Furthermore, it cannot do any harm.

Probably more important than any of these local measures is keeping the anterior nares clear by blowing and wiping the nose, as drainage in the natural direction is kept up in this way. Children must be prevented, as far as possible, from sniffing, as sniffing is probably more likely than anything else to cause extension of the inflammation to the middle ears and sinuses by preventing natural drainage and forcing the secretions into the Eustachian tubes and sinuses.

To sum up—the treatment of acute nasopharyngitis consists, briefly, in removal of adenoids, regulation of the life to diminish the vulnerability of the mucous membrane of the nose and nasopharynx, avoidance of exposure to contagion, isolation of the patient, confinement to bed for two or three days, and simple local treatment. If proper preventive measures are taken, babies and children will seldom have acute nasopharyngitis. If they are put to bed at once and kept there for two or three days, the nasopharyngitis will seldom be severe; complications will, therefore, be less common and, if they occur, less serious.

Ethmoiditis.—It is impossible to recognize slight inflammation in the ethmoid region. It is probable, indeed, that there is a mild degree of ethmoiditis in almost every case of acute naso-

pharyngitis in early life. It may be suspected when the symptoms are unusually severe and when there is more than the usual amount of puffiness of the eyelids; also when the nasal discharge evidently comes from high up in the nose. Persistence of the nasal discharge longer than would be expected after convalescence, especially if the discharge is unilateral, points strongly to a persistence of inflammation in the ethmoid tract. Occasionally the inflammation extends from the ethmoid cells to the orbit, with marked edema of the lids and pushing forward of the eye. These symptoms are accompanied by an elevation of temperature. As a rule the inflammation in the orbit quiets down and does not go on to suppuration, although in rare instances it may.

The presence of ethmoiditis, unless of a severe type, does not modify the treatment, which consists in keeping the nose clear and thus allowing free drainage. Treatment by a specialist may be helpful in the very severe and in the chronic cases. The tendency of inflammation in the orbit, secondary to ethmoiditis, being to quiet down and not go on to suppuration, it is important not to get too much excited and hence to operate when operation is unnecessary. Cold externally seems to favor the quieting down of the inflammatory process.

It is important to remember that ethmoiditis and inflammation of the orbit are never primary; that, if babies and children are properly taken care of and guarded against infection, they will not have acute nasopharyngitis; that, if when they have acute nasopharyngitis, they are put to bed and properly taken care of, they will rarely have a severe nasopharyngitis, and that they will, therefore, almost never have ethmoiditis and inflammation of the orbits.

Inflammation of the Frontal Sinuses and Maxillary Antra.—The frontal sinuses are so seldom developed in infancy and early childhood that extension of the inflammation to them in acute nasopharyngitis almost never occurs. It is presumable that the symptoms are the same in such cases as they are in adults. Infection of the maxillary antra is probably as common in infancy and early childhood as in late childhood and adult life. It al-

most never, however, is of a severe type, and practically never gives any recognizable symptoms. It is probable that the focus of infection, when there are repeated attacks of acute nasopharyngitis, is sometimes located in the maxillary antra. The treatment of acute nasopharyngitis is not modified by extension of the infection to the maxillary antra. It consists in keeping the nasal passages free and allowing free drainage. More active measures are never necessary.

Otitis media is a very common complication of acute nasopharyngitis in infancy and early childhood. The frequency diminishes steadily with increasing age. Extension of the infection to the middle ears is favored, as already stated, by the anatomic conditions in early life. It is less likely to occur if the nasal passages are kept free and there are no adenoids present. Babies and children do not have otitis media unless they have adenoids or acute nasopharyngitis; that is, otitis media is a preventable disease. Extension of the inflammation to the middle ear may or may not be accompanied by a rise in temperature. A rise in temperature should, however, always suggest the possibility that such extension has taken place. There is also likely to be an increase in the leukocytosis. This is of little importance, however, as there is a leukocytosis in acute nasopharyngitis, which varies without apparent cause. Babies are likely to act uncomfortable, be restless, moan and cry out sharply when the middle ear is inflamed. They are not likely to cry loudly and long at a time. Sometimes they become very dopey. They are not able to show where they are uncomfortable. They sometimes put their fingers to their ears. Babies that are uncomfortable from any cause also do this, so that it is of little importance. They are far more likely to rub their noses or put their fingers in their mouths. Tenderness over the mastoid process is almost never present. It is very difficult in babies to tell whether it is or not, because they are likely to cry when they are pressed anywhere. The symptoms in early childhood are a little more definite, as they apparently have more pain and are also better able to localize it. Their statements are, however, most unreliable and cannot be trusted. The only way in which

it is possible to recognize extension of the inflammation to the middle ears is by examining the ears regularly with an ear speculum, whether there are any symptoms pointing to the ears or not. When this is done, the trouble in the ears can be recognized early and treated at once. If it is recognized early and treated at once, it usually is a relatively simple matter. If it is not recognized early and properly treated, it is liable to be serious and to lead to further complications. Unfortunately, even when it is recognized early and treated quickly, it may also sometimes become severe and cause other complications. I do not wish to take up at this time the methods of examination of the ears in infancy and early childhood. It is sufficient to say that every physician who treats babies and young children should know how to examine the ears as well as he knows how to examine the throat and chest. Again, if a baby does not have acute nasopharyngitis or infected adenoids, it will not have otitis media.

If there is merely a little injection along the handle of the malleolus or around the periphery, dry heat should be applied externally. If there is pain, a few drops of a 1 : 1000 aqueous solution of one of the preparations of epinephrin or of a mixture of from 5 to 10 minims of phenol in an ounce of glycerin may be put in the ear. I doubt whether they do much good. Laudanum and oily preparations should never be used. From 5 to 20 grains of one of the bromids may also be given, according to the age of the child. If the drum is generally reddened, but the landmarks are still distinct or even if there is a little fulness of Shrapnell's membrane, it is usually safe to wait, unless the temperature is high and there is much pain. It is then wiser to operate. If there is much bulging of Shrapnell's membrane, much bulging of the drum as a whole or a localized nipple-like bulging, the drum should be incised. It should also be incised, if the drum looks thickened and hazy or yellowish, because, when the drum has these appearances, the tympanic cavity is usually filled with thick mucus or pus. When it is necessary to open the drum, it should be thoroughly opened. A long incision should be made, beginning in the lower portion and curving upward and backward behind the malleolus. It takes no longer for a long incision

to heal than for a short one. It gives much better drainage and there is much less chance of its closing too quickly. There is much to be said in favor of removing whatever adenoids may be present at the same time that the drum is incised. It undoubtedly favors drainage and the healing of the drum. It seems to me, however, rather more radical treatment than is necessary in most cases.

There is much difference of opinion as to the method of treatment to be used after the drum has been incised. As a general rule, it is wise, when the discharge is serous, not to irrigate the ear, but to wipe it out frequently and drain it with pledgets of sterile cotton. When the discharge is thick or purulent, it is wiser not to irrigate at once, but to wipe out the ears for the first few hours, and then to wash with sterile water, sterile physiologic salt solution, or a 2 per cent. solution of boracic acid, at a temperature of from 100° to 110° F., every few hours. It is most important to wipe the canal dry after it has been washed.

In the vast majority of cases in which the extension of the inflammation to the middle ear is recognized early and properly treated, that is, by prompt incision of the drum, recovery is prompt. Physicians are likely, however, to expect too rapid improvement after incision of the drum. It is true that in some cases in which the discharge is serous the temperature drops to normal within a few hours and the drums heal in a day or two. In my experience, however, such cases are the exception, not the rule. The temperature usually drops, but not to normal, and is likely to be elevated for several days, even in cases which are doing very well. Unless the drum heals within a few days, the discharge always becomes purulent. Some authorities believe that a purulent discharge always signifies extension to the mastoid antrum. This may or may not be so. However this may be, in the vast majority of cases there are no other evidences of mastoiditis, and no others ever develop. A purulent discharge of itself ought not, therefore, to be a cause of worry. In many instances the discharge continues for two or three weeks. It is undoubtedly true that the course of the disease depends largely

on the causative micro-organism. It is of no great advantage to know what this organism is, however, after it has got into the middle ear. If the doctor wanted to have an otitis media of a mild type, he might perhaps pick an organism of slight virulence. As he never wants to have an otitis media and, if he did, could not pick the organism, it seems useless to bother much about what it is.

When the discharge persists more than two, or certainly more than three weeks, the cause of the continuance is usually adenoids or an extension to the mastoid process. This is not always the case, however. It is very difficult to know, when the discharge from the ear persists and adenoids are present, whether it is advisable to remove the adenoids in order to favor drainage of the middle ear and thus hasten recovery, or to wait until the ear has healed and remove the adenoids later. Sometimes the ear will not heal unless the adenoids are removed. Sometimes the removal of the adenoids will increase the trouble in the ear and perhaps set up trouble in the other ear. Each case must be decided on its own merits. In general, I am rather inclined to take the chance of removing the adenoids at once if the discharge in the ear persists three or four weeks. I am not in sympathy with those otologists who advocate opening the mastoid process whenever the aural discharge lasts more than three weeks. It must be admitted, however, that they have much evidence on their side and that, in a certain number of instances, if the mastoid is not opened at this time, further complications develop. On the other hand, there are many cases in which the aural discharge persists much longer than three weeks and finally ceases without any other evidences of mastoid inflammation appearing and without any further extension. Here, again, each case must be decided on its own merits. It is wiser and safer, as a rule, to take the conservative point of view. The white count is, in my experience, of very little assistance in these cases. It is sure to be elevated anyway and the degree of the elevation is, especially in infancy, of very little assistance.

Mastoiditis.—The mastoid antrum is about the size of a pea at birth. The mastoid cells are not present at birth, but develop

during infancy, being numerous and of fair size at three years. The rate at which they develop is so variable that it is never safe to assume that even a young infant has no mastoid cells.

Severe mastoid inflammation is less common as a complication of otitis media in infancy than in early childhood, but may develop at any age. Symptoms which are suggestive of extension of the inflammatory process to the mastoid are—a higher temperature, a more profuse discharge, a longer continuance of the discharge, and a more marked leukocytosis than would be expected from the appearance of the middle ear. None of these symptoms are, however, more than suggestive, as there is nothing constant about the temperature, the amount of discharge, and the leukocytosis in otitis media. The leukocytosis is especially misleading in infancy, because it may be much elevated from slight causes at this age. The appearances shown by the Roentgen ray are also very deceptive and confusing. As already mentioned, continuance of the discharge for more than three weeks suggests very strongly involvement of the mastoid. Fulness of the posterior wall of the external auditory canal and enlargement of the posterior auricular gland are more important signs. They may, however, be due to other causes. Tenderness over the mastoid process points strongly to mastoiditis in childhood. It is of little importance in infancy, however, because it is almost impossible at that age to tell whether there really is tenderness or not. Moreover, even in childhood, it is often difficult to determine whether the tenderness is really in the mastoid or in the middle ear. Swelling and redness over the mastoid are later symptoms, and almost positive. It must never be forgotten, however, that they may be due entirely to external causes. Displacement of the external ear outward and forward is positive evidence of mastoiditis. The presence of mastoiditis should, however, always be recognized before the external ear is displaced, and it ought to be recognized before there is swelling or redness over the mastoid process. Failure to recognize it or, at any rate, to suspect it before these symptoms appear is evidence of either ignorance or carelessness on the part of the medical attendant.

It requires great judgment, when there is involvement of the mastoid, to decide whether the mastoid should be opened or not. There is no doubt that there is some little involvement of the mastoid antrum in almost every case of otitis media in early life. This involvement in the vast majority of instances is so slight that it is unrecognizable and of no importance. There is also no doubt that, in many other instances in which it is evident that there is some involvement of the mastoid, the inflammation clears up without operation, provided there is free drainage through the middle ear. It is very difficult to know whether an operation should be done in these mild cases. If the symptoms do not clear up, even in mild cases, if they are at all marked or if they are increasing, the mastoid should be opened at once, because, if it is, and external drainage is secured, the chances of the extension of the inflammation to the sinuses and meninges are much diminished.

Again, it must be called to mind that, if children are properly cared for and not exposed to contagion, they will seldom contract acute nasopharyngitis. If they are put to bed and properly taken care of when they have acute nasopharyngitis, they will seldom have otitis media as a complication. If otitis media is recognized early, when it develops, and the drum is incised, mastoiditis seldom develops.

The prognosis in mastoiditis, when the mastoid is opened early, is in general good, although, in a certain number of instances, the inflammatory process continues to extend. It may be noted here that some micro-organisms seem far more virulent than others, and that the same micro-organisms seem more virulent one year than they do the next. There is no doubt that in Boston and vicinity otitis media in early life is now more often accompanied by mastoid inflammation, thrombosis of the sinuses, and meningitis, than it was twenty or twenty-five years ago. There is also no doubt that in the past two or three years infections of the mastoid and deeper tissues have been more virulent and serious than they were even five or ten years ago.

Thrombosis of the Lateral Sinuses.—Although the petrosquamosal suture is not closed until after the first year, extension

of inflammatory processes in the middle ear to the sinuses and meninges is more common in early childhood than in infancy. The sinuses and meninges are very seldom involved unless there has been previous inflammation in the mastoids. Thrombosis of the sinuses and meningitis cannot be excluded, however, because the mastoid has not been involved. The early symptoms of thrombosis of the lateral sinuses are very indefinite. About all that can be said is that the child seems sicker than it ought to be and that the temperature is higher and lasts longer than would be expected from the local appearances in the ear and mastoid. Headache and tenderness above and behind the mastoid are suggestive. So is marked irregularity of the temperature. Chills are almost positive proof. The symptoms must necessarily vary with the severity of the process, depending on how much the clot is walled off, whether there is pus in the sinus and whether infection is entering the systemic circulation. It must never be forgotten, on the other hand, that a child may have thrombosis of the lateral sinus and not seem much sick, the only symptoms being a continued irregular temperature and an increase in the leukocyte count. It is very difficult to realize that a child who is sitting up in bed, playing with its toys, taking its food well and wanting to get up and about may have a thrombosis of the lateral sinus which, unless operated upon, will kill him in a few days. Such a picture is, however, not at all uncommon. The leukocyte count is, unfortunately, of relatively little assistance, because it goes up from such slight causes in early life and is certain to be elevated anyway from the otitis media and mastoiditis which preceded the thrombosis of the sinus. Immediate operation is obligatory whenever the diagnosis of thrombosis of the sinus is made. If an error is to be made, it is wiser to operate occasionally unnecessarily than not to operate when an operation is required.

Again, if babies and children are properly taken care of and protected against contagion, they will not have acute nasopharyngitis. If they are put to bed and properly treated, when they have acute nasopharyngitis, they will seldom develop otitis media, unless they have adenoids. If otitis media is recognized

early and the drum incised, extension to the mastoid process is unusual. If mastoiditis is recognized early and the mastoid process opened, extension of the inflammation to the lateral sinus very seldom occurs.

Meningitis is a very rare complication of otitis media in early life. There is nothing characteristic about the symptoms, which are those common to all forms of meningitis. Whenever meningitis is suspected, a lumbar puncture should be done for diagnosis. If there is meningitis, it is, of course, due to one of the pus-forming organisms. The spinal fluid, therefore, is turbid or purulent, contains a large number of polynuclear cells and a large number of the causative organisms. The diagnosis is easy. It must be remembered, however, that a moderate increase in the number of mononuclear cells or even the presence of a few polynuclear cells in the fluid, without organisms, even if there is a trace of globulin, does not necessarily mean meningitis. Such findings are not at all uncommon in connection with mastoiditis and thrombosis of the sinuses, and simply show toxic irritation of the meninges. I am inclined to think that they may occur occasionally in severe cases of otitis media without complications.

There is no specific treatment for this type of meningitis. Streptococcus vaccines and streptococcus antitoxin are, in my experience, useless. Repeated lumbar punctures may relieve some of the symptoms. I have never seen mercurochrome and similar preparations do any good. I have, however, known of an occasional recovery. I have always felt, however, that these recoveries took place not because of, but in spite of, treatment.

Again it must be remembered that, if a child does not have otitis media, it will not have a secondary meningitis.

Conclusions.—Acute nasopharyngitis in infancy and early childhood is very largely a preventable disease. Proper care of the child, avoidance of exposure to contagion, and the removal of adenoids, if present, diminish materially the morbidity of this disease. Proper care and protection of children with acute nasopharyngitis diminish the number of complications very markedly. Proper treatment of these complications as they arise diminishes their severity and the chances of their leading to futher compli-

cations. Severe complications should seldom develop as the result of acute nasopharyngitis. They may occur, however, in spite of the best of care from the beginning. When they do, the physician should always ask himself, nevertheless, whether or not some one is not responsible and, if there is, whether he is the one?

CLINIC OF DR. REGINALD FITZ

FROM THE MEDICAL CLINIC OF THE PETER BENT BRIGHAM HOSPITAL

CLINICAL PROBLEMS IN THE MANAGEMENT OF DIABETES WITH A REVIEW OF FOUR FATAL CASES

I, II. Diabetes and Tuberculosis.
III. Diabetes and Duodenal Ulcer.
IV. Diabetes and Infection.

I HAVE selected 4 unsuccessfully treated diabetic cases for this clinic in order to discuss certain phases of the diabetic problem which seem to me to be of very great practical interest.

Case I.—L. A., a real estate broker, fifty-one years old, was referred to the hospital on September 15, 1923, because of frequency of urination, incontinence, and 20 pounds recent loss of weight. He stated that he had been well all his life except for occasional minor illnesses like tonsillitis. He denied venereal disease, was not a drinking man, and considered himself in good condition except for recurrent attacks of bronchitis during the winter months.

In April, 1923, six months before he entered the hospital, he had noticed that his clothes were getting loose, and that though his appetite was good, he was nevertheless losing weight. He had noticed also that he had gradually become very thirsty and was making increasingly large amounts of urine which he seemed to have difficulty in controlling properly. He was a little concerned, too, because his memory was not as good as it had been, and because what he considered a normal day's work was now very fatiguing. For these various symptoms he finally consulted his doctor, who examined the urine, told him that he had diabetes, and referred him to the hospital.

He was a man 5 feet, 5 inches tall, with a supposedly normal weight of 225 pounds, but who weighed at entry 200 pounds. His physical examination was essentially negative except for a few scattered râles over both chests and for a considerable degree of peripheral arteriosclerosis. The blood-pressure was 145 systolic and 80 diastolic. The pulse rate was 70, and the oral temperature was normal on the afternoon of the first examination.

A single specimen of urine contained 5.6 per cent. of sugar and the blood-sugar concentration was .29 per cent.

He remained in the hospital for a few days while his urine was made sugar free and he was given instructions in regard to a proper diet. Incidentally, an *x*-ray plate of his chest was made which showed no significant abnormality and no signs of pulmonary tuberculosis. His case was so mild that he did not appear to require insulin.

A month later he reported again; this time he weighed 196 pounds. He was dieting carefully, the urine was sugar free, and he expressed himself as feeling perfectly well.

Four months after his first visit, on January 22, 1924, he reported a third time. He now weighed 194 pounds, had a normal urine, and a blood-sugar level of .12 per cent. He was feeling well, was dieting carefully, and appeared in excellent condition.

In spite of various follow-up notes, he was then lost track of for sixteen months, when the following letter was received:

Sunday, April 26, 1925.

My dear Doctor:

I beg to be excused for not sending you a reply on your recent communications to me. It was entirely carelessness on my part. I suppose I should have taken a little more time away from my business and paid you a visit. I now have my regrets that I did not come sooner.

I will make a special trip to see you on Wednesday the 29th inst. I hope that I will be able to see you at that time.

Yours sincerely,

L. A.

At this visit he weighed 200 pounds, and he stated that he was eating everything he wished. He had no definite com-

plaints except that his cough had been more bothersome than usual during the past winter and had been associated with a little pain over the left chest on deep breathing.

He looked in excellent condition. The urine contained only a trace of sugar. The blood-sugar concentration was .20 per cent. He was advised to pay more attention to his diet, to lose a little weight, and to report immediately if he did not feel better.

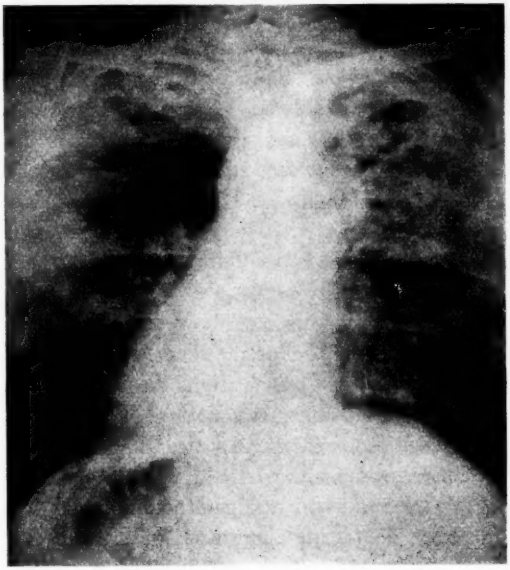

Fig. 139.—Chest radiograph of Case I. Advanced pulmonary tuberculosis developing in a diabetic while the patient was under observation.

Under the circumstances he seemed to be doing reasonably well and his clinical condition, eighteen months after treatment was first started, appeared satisfactory.

Another six months passed without news of him. Then, on October 14, 1925, a little over two years after his first visit, he turned up for the last time. He now weighed 164 pounds, having lost nearly 40 pounds since his preceding visit. He was eating everything, regardless of his diabetes, and the urine was

sugar free with a blood-sugar level of .18 per cent. He now had a troublesome cough. There were typical signs of tuberculosis through both lungs, the sputum contained tubercle bacilli, and the *x*-ray revealed extensive infiltration of the upper two-thirds of both lungs with cavity formation. He went down hill rapidly, dying on March 5, 1926.

It is worth while to consider for a moment the association between diabetes and tuberculosis. This combination of diseases is of not infrequent occurrence and almost always develops insidiously. The medical service of the Brigham Hospital for several years has made it a rule to *x*-ray the chests of all diabetic patients admitted, and in this way a large number of tuberculous diabetics have been recognized who might otherwise have been overlooked. The tuberculosis is prone to develop around the lung hilus and often becomes far advanced before it produces characteristic physical signs. There may be no breaking down of the lesion, so that tubercle bacilli do not appear in the sputum, and no febrile reaction may occur.

I have not presented this case, however, in order to discuss tuberculosis, but in order to illustrate another feature. Here was a man, who, while under observation, developed an extensive pulmonary disease. This lesion was noticed only in its end-stages. Had it been recognized earlier, the patient's life might have been saved. Because he looked well, held his weight, remained essentially sugar free, and had no definite complaints, the patient was considered to be getting along well, and his tuberculosis was not discovered in its early stages. Those of you who have been in the habit of making Staff Ward Rounds with us may remember that Professor Christian once remarked last winter that he was seriously considering writing a paper on the possible dangers to any patient in having a chronic illness easily diagnosed. His point was, that patients with a chronic malady often develop very serious superimposed diseases which in the presence of an unmistakable primary illness, are entirely overlooked. On the whole, we are taught and properly, to explain a clinical syndrome by a single diagnosis. This teaching, however, does not justify the assumption that in the presence of a chronic disease, other

diseases cannot develop. Therefore, patients with any chronic disease must have a fresh history and, from time to time, a complete physical examination, made as nearly as possible from a fresh point of view, in order that any new complications may be brought to light.

I think Dr. Christian would consider this case a good example of what he had in mind. In reviewing the record it is reasonable to assume that the patient's letter of April 26, 1925 was written because he was not feeling well. Had he, at that date, been considered as a new case, been more carefully examined, with due emphasis placed upon the story of cough and pain in the left chest, it is entirely possible that an early tubercular process might have been then discovered and that an unnecessary diabetic death might thus have been avoided.

Remember, therefore, that in the management of diabetes it is necessary to be constantly on the watch for complications. Diabetics must have repeated periodic physical examinations at least two or three times a year, and their general physical condition must be observed as carefully as are the blood and urine.

Case II.—R. C., an engineer, fifty-two years old, entered the hospital on July 24, 1923. His previous history was unimportant. About a month before entry he suddenly noticed polyuria, polydipsia, polyphagia, and loss of weight. At entry the diabetes was immediately recognized and he was advised to undergo a course of treatment.

His physical examination, including an *x*-ray of the chest, was negative. The urine contained $2\frac{1}{2}$ per cent. of sugar, the blood-sugar level was .25 per cent. He responded well to treatment, and on August 14th was discharged, weighing 112 pounds, and feeling well, on an adequate diet without insulin and with a fasting blood-sugar level of .14 per cent.

A month later he reported, sugar-free, well pleased with his condition, and weighing 124 pounds. He was then lost track of until June 9, 1925, nearly two years after his first admission. In the meanwhile he had been taking care of himself, getting along well for about twelve months, and then commencing to have

difficulty in keeping sugar free. He managed his case by starving himself when the urine showed sugar, then eating a liberal diet until the sugar reappeared. Unfortunately he was compelled to fast more often than he was able to eat, and thus found himself becoming progressively weaker and thinner.

At his visit on June 9, 1925 he weighed 106 pounds. The urine contained 3 per cent. of sugar, and the blood-sugar level was .31 per cent. Physical examination of the chest showed dulness at the right apex with persistent râles, the sputum contained tubercle bacilli, an *x*-ray film showed a characteristic area of infiltration in the lower portion of the right upper lobe. Despite sanitarium care and insulin he continued to go down hill, dying on April 9, 1926.

This case illustrates another aspect of the diabetic problem which is worth considering at some length. It is the present custom for hospitals or doctors to train diabetic patients in regard to the management of their own cases. The patients are taught how to weigh and measure food, how to analyze urine, how to care for themselves in emergencies, and it is not uncommon to encounter diabetics so trained who say they would prefer to conduct their own cases until a specialist can be called rather than to rely upon the judgment of their own general practitioner whose diabetic knowledge they consider limited.

While this plan of intensive instruction of patients may be a proper one to follow in many instances, yet it is by no means entirely safe. The patient in question was an intelligent, hard-working man. He was unwilling to attend a free diabetic clinic and too economical to spend money on unnecessary doctor's visits. He considered that he had learned most of what there was to be known in regard to the management of diabetes, as he had carefully read and studied the simpler diabetic text-books. When it came to his own case, his treatment was successful for several months, but when there arose a difficulty in keeping sugar free he still continued to rely upon himself with the apparent result of a resistance so lowered that tuberculosis developed. It would have been better treatment, perhaps, to have

taught this patient to be less sure of himself, thereby obviating the danger of his considering himself infallible.

Certainly it is well for diabetics to know a good deal about their disease, but, on the other hand, they must not be taught too much. They must realize the necessity for constant medical supervision. The medical profession at large must know more about diabetes than those whom they are called upon to treat, and general practitioners must not regard diabetic therapy as a narrow specialty to be competently handled by only a few highly trained men.

I believe that this case received imperfect diabetic treatment because, although we gave this patient a good diabetic education, we erred in placing undue emphasis on his share of the job and in failing to impress on his mind that proper medical supervision was an important part of the therapy. I present this case, therefore, as a second failure because of medical mismanagement in the treatment of diabetes.

Case III.—H. R., a dairy merchant, fifty-one years old, entered the hospital on September 18, 1923, complaining of pain in the upper abdomen. He was known to have had a mild diabetes of about six years' duration which had been easily controlled by moderate dietetic restriction. His chief complaint was a gnawing indigestion which had persisted for several months.

He was a large man, weighing 190 pounds. Routine physical examination was normal. The urine on several determinations contained no more than a trace of sugar, and the fasting blood-sugar level fluctuated around .12 per cent. A gastro-intestinal *x*-ray series revealed a duodenal ulcer as cause for the digestive symptoms, accompanied by marked hyperacidity as shown by gastric analysis. There were no signs of pyloric obstruction after the barium or Ewald meal.

The patient was treated by the Sippy method and felt considerably better after remaining in the hospital six weeks.

He reported again on January 12, 1924, saying that until two weeks before he had felt well. Recently, however, in spite of alkaline powders and diet, his stomach had been bothering

him again and he felt discouraged, although he had gained 10 pounds in weight since leaving the hospital.

His physical examination was unchanged. He looked healthy and in good condition. The urine had only a trace of sugar in it, and the blood-sugar level at 4 P. M. was .11 per cent. A sample of gastric juice obtained at this time contained no free hydrochloric acid. On the whole, both the diabetes and the duodenal ulcer appeared to be under good control, and the patient was advised to continue as he was with the expectation that he would improve as time went on.

Being dissatisfied and impatient with this method of procedure, however, he consulted another doctor, who told him that an operation afforded his only chance of permanent benefit.

Accordingly, on January 29th (a little over two weeks after his last visit to the Brigham Hospital) he had a laparotomy. On opening the abdomen there was found a mass of fat omentum which made it difficult to visualize the region of the duodenum. There were many adhesions from the duodenum to the gall-bladder. After these were freed, down in the depths of the incision there was demonstrated what appeared to be an area of indurated, contracted ulcer with a crater. This area was on the first portion of the anterior wall of the duodenum, and from it there had arisen many adhesions to the gall-bladder drawing the gall-bladder over toward the duodenum. The duodenum was fixed in the depths of the cavity so that there was no question of a plastic operation, and a posterior gastro-enterostomy was made. The patient developed bronchopneumonia following operation and died within a few days.

I have presented this case for three reasons. In the first place, I want to remind you that the presence of diabetes, no matter how mild or how well controlled it may be, exaggerates the risk of surgery. While diabetic patients can be prepared for operation and can usually be carried through surgical procedures safely, yet a slightly increased hazard remains in each case and no diabetic patient should be considered an entirely safe operative risk nor be subjected to any operation but that of necessity without due deliberation.

I have presented this case, also, because it represents to my mind an example of the high cost of failure in the practice of medicine. I have selected it, too, in order to remind you that in spite of the scientific advances which have been made recently in the treatment of diabetes, you must never forget the personal equation of each patient, but must always remember that he is a human being—a man—and *NOT* a test-tube.

The successful practice of medicine depends upon a proper blending of medical knowledge and personality. The doctor who undertakes the treatment of patients with a chronic malady must assume total responsibility for managing the lives of those patients, and he will never make a success of his work unless he can impress upon his clients the soundness of his medical advice so strongly that they are willing to follow in every detail the treatment and method of life outlined. In the treatment of diabetes, particularly, does the doctor's personality count. The disease itself tends to limit the patient's physical and mental activities to a certain extent, the diet becomes remarkably monotonous, and unless one has talked with intelligent patients one can never fully realize how important a part in the pleasures of life is played by well-cooked and palatable foods. The doctor caring for diabetics in an ideal way must manage to become a never-failing support to his patients and must succeed in steering them away from all kinds of temptations and evils.

This man after his visit in the hospital came to my office in order to see me personally. I talked his case over with him, tried to explain to him what his medical situation was, and what, in my judgment, was the proper course for him to follow. The end-result clearly shows that I was unable to make any deep impression upon him, so did not practice the art of medicine successfully and thus failed to avert an unnecessary diabetic catastrophe. This case is presented, therefore, to warn you that no matter how scientific your treatment of diabetes may be you will fail in the long run unless you are good doctors in the old-fashioned sense of the word.

Case IV.—A. D., a candy packer, seventeen years old, was referred to the Brigham Hospital on April 24, 1925, because of diabetes. Her past history was negative except for frequently recurring attacks of tonsillitis. Her present history was of interest because in connection with her occupation she found herself under constant temptation to eat candy, and estimated that for several months she had been eating at least a pound of candy each day.

Until three months before she had been feeling well. Then for no apparent reason she began to lose weight. This did not disturb her. The diabetes was discovered at a Life Insurance examination and she was sent to the hospital for treatment.

The physical examination was entirely negative except for tonsils which were described as being large and cryptic. The admission specimen of urine contained 4 per cent. of sugar which quickly disappeared under diet.

She remained in the hospital for twelve days and was then discharged with instructions in regard to her diet. She was sugar free, with a fasting blood-sugar concentration of .14 per cent. and on an adequate diet without insulin. It is perhaps of some significance that her case seemed so mild that she never received any insulin.

She reported to the Out-Door Department at monthly intervals, always having a sugar-free urine, looking and feeling well, holding her weight at a level between 105 and 110 pounds, and apparently taking excellent care of herself. On August 25, 1926 the record states: "Sugar free all the time, feels fine, adheres to diet."

Three weeks later, on September 16, 1926, she developed a sore throat. She soon became weak and drowsy, and finally comatose. She was brought to the hospital on September 20, dying within forty-eight hours of a general infection.[1]

This case is presented as another failure in diabetic therapy and again to emphasize Dr. Christian's observations on the possible dangers to a patient in having a chronic disease easily recognized. You will remember that this girl had repeatedly

[1] The necropsy revealed an extensive bronchopneumonia as cause of death. The tonsils were not examined.

suffered from attacks of tonsillitis before she developed diabetes, and that the only definite abnormality noted in her physical examination lay in the tonsils. She entered the hospital, however, for diabetes—an easily recognized malady in her case since she was a great candy eater and the urine specimen at admission was full of sugar. Consequently the entire attention of the hospital staff, was apparently focused upon the diabetes. The result was that while the diabetes was adequately treated, the tonsils were left *in situ*, to become the path of entry for the infection which caused her death. It is very possible that if they had been removed when she first came under supervision her death might have been prevented.

Any infection in diabetes is always serious. I have already mentioned the possible importance of tuberculosis in this connection. I should like to add that foci of chronic infection such as infected teeth or tonsils should always be searched for and should be eradicated when they are found to be present. Not only may they serve as a portal of entry for a general infection as in this case, but they may also cause a definite lowering of tolerance and thus exaggerate the apparent severity of a given case. Other organs with chronic infections, such as the gallbladder, appendix, prostate or tube, should be treated appropriately; better results are often obtained by radical rather than conservative treatment.

CONCLUSIONS

I have described four unsuccessfully treated diabetic cases in order to discuss a few phases of the diabetic problem which are often turning up and which seem to me worthy of comment. I have tabulated the various points which I have tried to bring out in order that you may leave this clinic with a concise idea of what I have particularly wished to emphasize.

1. Tuberculosis is a common complication of diabetes and one frequently overlooked. Therefore, make a careful examination of all diabetic chests and have *x*-ray pictures taken in all suspected chest cases. Be on the lookout for all possible foci of infection, and if any are present, have them removed. An area of

infection not only lowers tolerance, but may serve as the portal of entry for a fatal septicemia.

2. The course of a diabetic case must be carefully observed. A complete physical examination of each case should be made at least twice a year. Normal blood and urine sugar determinations, a constant body weight, and a general good appearance of the patient do not by necessity exclude serious complications.

3. Diabetic patients not only must be taught how to take care of themselves, but must also be made to realize that the conduct of their cases should be carried out under medical supervision. Each case should report at least four times a year, and oftener if necessary. No case must feel that he knows as much about diabetes as his physician.

4. Diabetes cannot be best treated in a machine-like fashion. Its most successful management depends on last analyses upon a good doctor; the doctor's personality counts almost as much as does his medical knowledge. He must use common sense and tact in the handling of such cases, have an understanding of his patients' mental reactions and a personality so impressive that his instructions will be carried out perfectly and faithfully by each patient who comes under his care.

CLINIC OF DR. FRITZ B. TALBOT

MASSACHUSSETTS GENERAL HOSPITAL

EARLY TUBERCULOSIS OF THE MESENTERY LYMPH-NODES. REPORT OF TWO CASES

Introduction.—Every now and then a practising physician is puzzled by the children who have persistent symptoms of indigestion without demonstrable cause, who do not respond as they should to dietetic treatment; in whom all anaphylactic causes of the indigestion have been eliminated; and in whom the symptoms, although pronounced enough to keep the child in bed much of the time, are sufficiently severe to cause the parents much worry and the child considerable discomfort. The following case is an example of one of these children:

Case I.—A boy aged seven and a half years was first seen in 1923 at the age of three years with a history of having had loose movements for over a year. The previous spring he had had a severe diarrhea which had lasted for a week. He was put on a limited diet and the frequency in the stools diminished so that he had only two a day—the first one being loose and the second one formed. The stools were as a rule light colored. At intervals he had five to six movements a day and was continuously troubled with gas.

His physical examination was completely normal, except that the abdomen was protuberant. The heart and lungs were normal. The liver and spleen were not felt. It was thought at first that he had a case of colitis.

During the course of his third summer he improved, and his stools were mostly normal, but at times had a fermented odor.

In the fall he had not gained much weight, did not sleep well, had dreams which disturbed his sleep, and was again having loose movements which did not seem to have any relation to the diet. It was found at that time that his movements could be improved by the administration of milk of bismuth and the bulgarian bacillus. During the fall he had improved, but every few weeks would have a digestive upset in which the stools became loose and acid. This came on without any relationship to his diet. At times he complained of abdominal pain.

During the winter the movements were usually good, but he did not gain weight and was constipated. Late in the fall an anteroposterior pad was applied to his abdomen on account of the protuberance, gas, and distention. Since then he complained very little of gas, but early in the spring of 1924 he was troubled much at night by bad dreams. Associated with this was slight elevation of temperature up to 100½° F. Although his appetite was good, he gained very little and during the spring was skinny, fussy, and whiney. He continued to run a slight temperature and it was finally decided to investigate him by *x*-rays.

The *x*-ray of the abdomen showed several calcified glands in the right flank, and of the chest slight hilus thickening with a few peribronchial glands, which were not calcified. Since the hygiene was excellent and it was possible to have him out in the sunlight, he was kept out-of-doors most of the time and his temperature gradually diminished so that he rarely, at this writing, has an elevation of temperature. He has continued to gain weight and is to all intents and purposes well.

A second case of the same sort is as follows:

Case II.—A boy, age six years, had the following history: In the spring of 1926 he complained of pains in the stomach and discomfort in the bowels. His abdomen had been previously noted to be prominent. A careful examination of the abdomen did not reveal any spasm or tenderness, nor could any masses be made out. His examination otherwise was negative.

The pains in the abdomen recurred off and on and last fall he had clay-colored stools. At that time an *x*-ray showed en-

larged glands which were partly calcified in the right lower quadrant of the abdomen.

The striking feature of these 2 cases which are taken as illustrations is the indefinite group of symptoms associated with pathology of the mesentery glands. In the first case the outstanding symptoms were diarrhea or loose movements, gas and

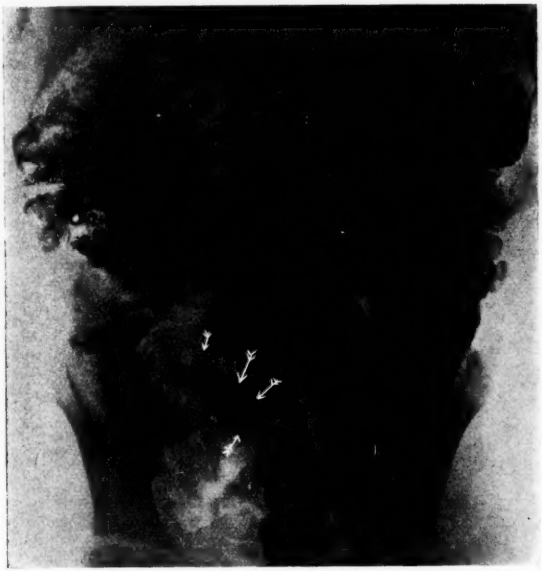

Fig. 140.—*x*-Ray of Case II showing very early glands without much sign of calcification. White arrows point to the shadows thrown by the masses.

pain, which had no connection with the diet, and more or less continuous low fever. In the second case, indefinite symptoms of pain which caused the child to be examined for appendicitis, little or no fever, and the one instance of clay-colored stools. Both children were high strung and very active. In both instances the abdomen was more protuberant than usual for boys of the same age. In neither instance did the physical examina-

tion show anything abnormal except the large abdomen. In both instances the diagnosis was only made possible by means of the *x*-ray examination.

The usual text-book descriptions of mesenteric tuberculosis are of the disease in the more advanced state in which masses can be felt and in which there may or may not be ascites. This type of abdominal tuberculosis is quite easily recognized, but

Fig. 141.—Showing more pronounced shadows and early calcification in another patient.

the early stage is very difficult to diagnose. It must be differentiated from the subacute or chronic appendicitis, cyclic vomiting, and indigestion. In some instances demonstration of tubercle bacilli in the stool gives a positive diagnosis. This, however, is only occasionally possible. The Pirquet or intradermal tuberculin reaction is sometimes useful, but it is not to be depended upon. A white count is not always very helpful, but the differential count helps to differentiate from subacute appen-

dicitis; a high polynuclear leukocytosis suggesting appendicitis. If there is any involvement of the lungs or evidence of the enlargement of peribronchial glands, tuberculosis must be ruled out. Chronic infection due to large tonsils and adenoids may produce symptoms similar to those seen in these cases, but are rarely associated with pain. The symptoms practically always disappear when the adenoids and tonsils are removed. Cyclic

Fig. 142.—Showing single groups of calcified glands which indicate healing.

vomiting is practically always associated with vomiting and rarely with pain, so that the fact that the prominent symptom of mesenteric tuberculosis is pain rather than vomiting helps to differentiate these two conditions.

The diagnosis depends mainly upon recurrent attacks of pain and protuberant abdomen, a low and persistent temperature in an irritable child who is not as fat as he should be and may be somewhat emaciated. The final diagnosis depends upon

positive x-rays finding of glands and a positive tuberculin or the isolation of tuberculin bacilli from the stools.

In order to obtain a good x-ray picture of the abdomen in these cases, the intestines must be free from gas and the bowels must be more or less empty, in which case it is often possible to get clear evidence that glands are present. I have not been able to find any data which tells how early it is possible to recognize pathologic mesentery glands. They are, of course, most easily

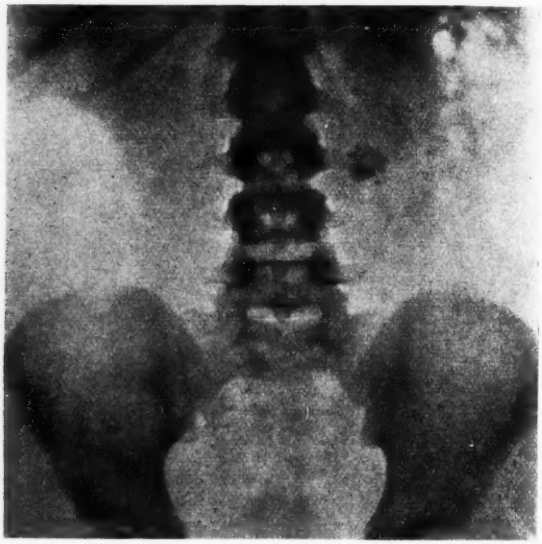

Fig. 143.—Showing single groups of calcified glands which indicate healing.

demonstrated after they become calcified. It does not seem probable that calcification takes place in the early stages of the disease; it therefore is not to be expected during the first month or two of the symptoms.

Calcified glands are easily recognized in the later stages of the disease.

The light-colored stools or clay-colored stools, which very often are noted in these cases, are largely made up of fat and are known

as "soap stools." In normal digestion the fat is absorbed through the lymphatics. When the lymphatics become blocked by disease the fat is unable to pass through, and if enough glands are involved in the proper locations the absorption of fat is seriously interfered with. If the diet contains large amounts of fat in an endeavor to make the child gain weight, a secondary indigestion may result and intensify the symptoms. It can only be cured by giving the child a fat-free diet. In general, the diet of these children should contain only limited amounts of fat. When the abdomen is distended it is probable that even a few diseased mesenteric glands can disturb the intestinal function enough to retard the passage of gas and feces. The intestines become distended and sluggish as a result. This was exemplified in the second case in whom the large intestine was definitely atonic and the peristalsis retarded. The gas in the intestines caused abdominal distention which was so striking in the physical examination. This is usually relieved and the symptoms are markedly improved by the application of an anteroposterior belt which supports the abdominal wall and prevents the intestinal distention.

Since a tubercular infection is the cause of the disease, the treatment outline must be for the purpose of curing the tuberculosis. The usual tonic measurements may be undertaken. Heliotherapy, of course, is of the most importance. This should be used with care and the dosage regulated carefully, because too much sunlight can cause symptoms and retard recovery. In the summertime the child may be exposed to the direct sunlight, commencing first with ten minutes a day, to the arms and legs only. The exposure may be increased ten minutes a day until the greater part of the body is exposed for several hours. During the wintertime the child may seek sunlight in the south or receive graduated doses of the ultra-violet ray from the mercury-vapor quartz lamp.

Result of Treatment.—The result of treatment of these early cases of tuberculosis of the mesentery glands has been most satisfactory. In the majority of instances there is continued and progressive improvement. This may be checked

up by x-ray examinations of the glands, which shows the rate of calcification of the glands.

It is of great importance to recognize and diagnose cases of this type at an early date before the glands break down and before the disease becomes so generalized that it cannot be controlled by any method of treatment.

CLINIC OF DR. SOMA WEISS

THE BOSTON CITY HOSPITAL*

THE CLINICAL ASPECT OF OBSTRUCTIVE DISEASES OF THE COMMON BILE-DUCT

I INTEND to demonstrate this afternoon a few patients with instructive observations on occlusive diseases of the common duct. I shall also attempt to discuss certain problems related to the recognition of these diseases.

It is rather unfortunate that obstructive diseases of the common bile-ducts are often considered surgical problems. The interest of the physician in the diagnosis of these conditions should be keener than that of the surgeon. It is the practitioner to whom the patient turns for advice with vague complaints related to the stomach, or with painless jaundice, or with an accidentally discovered abdominal tumor; and it will depend on his knowledge and advice whether or not the life of the patient is saved. It is also probable, that with increasing interest on the part of physicians, our clinical ability to recognize and differentiate these conditions will improve.

While the clinical aspects of liver and gall-bladder pathology have received considerable interest during the past few years, very little progress has been made in the clinical recognition of common duct pathology. The explanation of this discrepancy of progress may be found in the fact that while laboratory methods yield practical help in the diagnosis of certain diseases of the liver and of the gall-bladder, they fail to throw light on pathologic changes of the common bile-duct. The harmful effect of the present-day tendency to depend on laboratory methods in diagnosis and to neglect the careful analysis of symp-

* From the medical service of Francis W. Peabody.

toms and signs is therefore more obvious in case of the diseases of the common bile-duct than in diseases of the gall-bladder. After reading the clinical studies of physicians of the last two decades of the past century, one is apt to conclude that not only have we made no progress in the recognition of diseases of the common bile-duct, but we have actually lost some of the clinical skill possessed by our masters.

It is important that we should have a proper concept of the value and interpretation of clinical symptoms and signs, as well as of laboratory methods. The lack of recognition of the limitation of a clinical sign often causes more harm than the total lack of knowledge of the sign. This principle holds true also for laboratory methods. It is worse to apply a test without appreciating its limitation than not to know the test at all. This principle, which seems to be so obvious that one may be criticised for mentioning it, is nevertheless often not appreciated. When a new method, especially a simple one is introduced, it takes several years before the test occupies its proper place in the medical instrumentarium. However, hardly do we become convinced of the great limitation of one method before another is introduced and the same situation again presents itself.

Laboratory methods used in diseases of the biliary system may serve as an illustration. After the introduction of the Meltzer-Lyon test, for example, physicians and surgeons relied on it as a method of differentiating various types of pathology of the biliary system. Scarcely had the great limitations of this method, so far as diagnosis was concerned, begun to be appreciated when other methods were introduced, and again there was a tendency to overemphasize their clinical significance. Some of these methods are of great aid provided they are properly interpreted. The recent methods of gall-bladder visualization signify great advance in diagnosis, especially if they are combined with careful clinical observations. The recent methods for measuring the bile-pigment content of the blood-serum are of also great service to investigators and physicians as an objective means in following the condition of the patient. The practical significance of the icteric index and the van den Bergh test for

estimating bilirubin content of the blood as an aid in diagnosis is nevertheless limited; and I believe that just at the present time these two methods, as far as their value in diagnosis is concerned, are overestimated. One should not forget that the color of the skin is a rather sensitive and reliable index to the bile-pigment content of the tissues. If a patient is jaundiced and the bile content of the stools markedly reduced, it is obvious that he is suffering from obstructive jaundice. The van den Bergh test can only confirm this clinical observation. The next and most important problem in diagnosis is to decide whether we are dealing with a stone in the common duct or with a tumor of the head of the pancreas pressing on the common duct, or with a cirrhosis or toxic degeneration of the liver. What we, as physicians, want to know is whether or not the patient will recover spontaneously; whether or not surgical interference is indicated in re-establishing free bile flow, or whether the patient is suffering from an incurable disease. In this, the most difficult and most important problem, neither the icteric index nor the van den Bergh test will help. In recent publications on the diagnostic value of the van den Bergh test it is repeatedly stated that following a "gall-bladder attack" or passage of stone, occasionally the bile-pigment content of the blood may be increased as measured by the icteric index or by the van den Bergh test, without obvious jaundice of the scleræ or of the skin. Such clinical conditions indeed occur. Nevertheless, it is to be remembered that identical situations may exist with a fleeting, early duodenitis or cholangitis in which the symptoms may be similar to a "gall-stone attack"; and therefore the increased bile-pigment content of the blood under such conditions will not necessarily indicate gall-stones. One is apt to conclude from the fact that occasionally the skin may not show changes in color when blood-serum shows an increased bile-pigment content, that jaundice of the skin as compared with measurements of the bile-pigment content of the blood is a crude and late sign. This conception is faulty, however. I wish to emphasize here, therefore, a point which may be of practical value. In patients with chronic or intermittent disturbances of the bile-

pigment metabolism I have observed repeatedly that although the blood-serum showed no increase in the bilirubin content as measured by the icteric index and by the van den Bergh test, the skin of the patients showed changes in color. Such a condition existed in patient II, for example, as will be shown later, who had probably had a large stone in the common duct for nine months. The icteric index of this patient was repeatedly within normal limits, although the patient and his family noted a distinct change in the color of the skin. Following the spontaneous passage of the stone the yellowish-bronze color of the skin which was present for several months disappeared within three weeks.

The fact that the skin may show pigment changes, while the bile-pigment content of the blood-stream is within normal limits, is in harmony with well-recognized principles of physiology and pharmacology. The majority of chemical substances, if introduced into the body, leave the blood-stream rapidly, and often instantly. These substances will show a persistent increase in the blood only if the rate of injection is greater than the capacity of the tissues to absorb them, or after the tissues become relatively saturated. Clinical observations indicate that the bile-pigments behave in an identical manner. Persistent pigment changes of the skin in the presence of normal bile-pigment content of the blood may be present therefore in chronic disturbances of the bile-pigment metabolism.

I wished to spend a little time in discussing these general points, as I believe that it is of the utmost importance that physicians should realize that in diagnosing diseases of the common bile-duct, a carefully taken anamesis and physical examination, or in other words, the proper analysis of symptoms and signs exhibited by the patient, are the greatest aid for the physician. All the results of laboratory methods should be looked upon as only supplement to clinical evidence.

Before demonstrating the patients it may be of help as a short recapitulation, to enumerate the various conditions, which may produce obstruction of the common bile-duct. The classification is given according to Herbert French:

I. Causes of Jaundice Due to Obstruction of the Larger Bile-ducts, Especially of the Common Bile-duct

A. *Causes within the duct:*

Gall-stones.
Inspissated bile.
Parasites { Hydatid cysts. Distomata. Ascarides.

B. *Causes affecting the wall of duct:*

Catarrh of the mucous membrane of the duct.
Catarrh of the mucous membrane of the duodenum involving and obstructing the ampulla of Vater.
Catarrh of the pancreas spreading to and involving the ampulla of Vater (chronic pancreatitis).
Carcinoma of the duct.
Cicatrization following ulceration of the duct.
Congenital obliteration of the duct.

C. *Causes compressing the duct from outside or invading it from outside:*

Peritoneal adhesions.
Enlarged portal lymphatic glands:
(*a*) Secondary malignant.
(*b*) Lymphadenomatous.
(*c*) Tuberculous.
(*d*) Leukemic.
Tumors of the liver.
Tumors of the pancreas.
Tumors of the duodenum.
Tumors of the stomach.
Tumors of the colon.
Tumors of the right kidney.
Tumors of the suprarenal capsule.
Tumors of the ovaries.
Tumors of the uterus.
Tumors of the omentum.
Aneurysm of the hepatic artery.

A detailed account of the pathologic characteristics of each of these conditions is outside of the scope of this clinic. I shall, therefore, only briefly summarize the principles to be followed in diagnosing obstructive diseases of the common bile-duct.

If the clinical findings indicate obstruction of bile flow, the first thing to decide is whether or not the patient is suffering from a type of obstruction which can be relieved by surgical interference. The differential diagnosis is raised, therefore, between on the one hand stone or stricture of the common duct, parasites in the common duct, pressure due to localized non-malignant growth from outside of common duct, and on the other hand obstruction due to diffuse malignancy, cirrhosis of the liver or yellow atrophy, cholangitis, etc. One should remember that stone in the common duct is not the only obstruc-

tive disease of the common duct which is amenable to surgical interference. It is erroneous to think therefore that after concluding that a patient is not suffering from a stone of the common duct the practical aspect of the diagnosis is settled—that is to say, to consider that the patient is not suffering from a disease which may be benefited by surgery. While stone in the common duct is the most frequent surgical disease of the common duct, obstruction of the common duct due to parasites in countries of the far East and of South America is relatively not rare, and not unknown even in this country. Stricture of the common duct relieved by surgery is not as rare a condition as was considered in the past; compression of the common duct from outside, due to pressure of benign tumors around the duct, occurs more frequently than we are able to recognize clinically at present.

As stone in the common duct and malignant tumors are the most frequent causes of obstruction of the common duct, the differential diagnosis between these two conditions is of great importance. Omitting here the usual clinical manifestations of these two conditions, certain general considerations in the differentiation may be summarized here.

1. Stone is more apt to be associated with *fluctuating jaundice.*

2. *Palpable gall-bladder* suggests malignant growth (Courvoisier's law).

3. If *ascites* is present, this speaks for malignancy.

4. *Fever* is in favor of stone.

5. *Pain*, especially if sharp and intermittent in nature, occurs classically with stone in the common duct.

These axioms should be considered as such only with limitations. While they may be useful in "statistical diagnosis," they may be misleading in the diagnosis of a given patient. I shall add therefore the following reservations:

1. Malignancy, especially annular carcinoma of the large bile-ducts, may be associated with fluctuating jaundice. Similarly, metastatic lymph-nodes pressing on the common duct may produce jaundice of changing intensity. The probable explanation of this phenomenon is that the growth of malignant tumors

progresses in no continuous manner, but often with temporary retrograde changes. It is also probable that after early partial occlusion certain mechanical readjustments may occur on the part of the common duct.

2. While the Courvoisier principle holds true in a certain percentage of patients, it is often not reliable. It is significant that as Neumueller of Vienna, on the basis of an analysis of a large amount of clinical material points out, the Courvoisier law is especially apt to fail in patients who exhibit obscure clinical manifestation, and in whom the differentiation between stone and malignancy is difficult. Indeed he reports a failure of this principle in a third of such patients.

3. Ascites if present is a useful differentiating sign. It is well recognized, however, that extensive malignant growth of the liver or the pancreas is frequently not associated with ascites.

4. Fever may be present in cases of malignant growth of the liver.

The following patients will serve to demonstrate some of the clinical principles just mentioned. They are also presented here because of somewhat unusual clinical findings and because of the unusual pathologic condition found at operation or at autopsy. In the case reports the unessential findings are omitted.

Case I.—Healed and Calcified Miliary Tuberculosis of the Liver and Peritoneum. Healed Tuberculosis of the Spine. Calcified Portal Lymph-nodes Obstructing the Common Duct. Recovery After Operation.—This patient, who as you see looks normal at present, is T. M., an American painter of fifty-two. He entered the Fourth Medical Division of the Boston City Hospital on September 17, 1926. His chief complaint was loss of strength and jaundice.

About two months previous to admission this patient noticed gradual loss of strength, without loss of weight. Later, about two weeks before entrance, he noticed that his urine was dark brown in color. At the same time he developed itching over the entire body, more marked over the face. About a week before coming to the hospital his eyes and face became yel-

low, and later he noticed that his stools were light colored. Frequently he felt nauseated, and at times vomited. At no time did he experience abdominal pain. There were no chills and he did not feel feverish. He had never been jaundiced before. It may be of interest to mention that the patient had been doing house painting for about thirty-two years. Three years ago he was admitted because of lead colic. He did not suffer from abdominal pain since that time. He has been constipated lately.

He married twice; his first wife died during "child-birth," leaving behind two healthy children. The second wife has borne three children and has had one or two miscarriages.

As a child the patient had scarlet fever. Fifteen years ago he was in this hospital with acute otitis media and with a suppurative infection of the mastoid. The rest of his history is unessential.

The patient was a fairly well-developed male, whose skin and scleræ were yellow. There was a slightly haggard expression of the face. He was lying flat in bed, his respiration was natural, and he did not seem to be in distress. Over the gums there was a bluish line. The teeth were in poor condition. The head was normal otherwise. Similarly, the neck, lungs, and heart were normal. The brachial, radial, and temporal arteries were tortuous and thickened. The radial pulses were full and bounding. The blood-pressure was 210/150. The abdomen was slightly protuberant and soft. There was but slight resistance with some tenderness over the right upper quadrant. No mass was palpated in the gall-bladder region. There was a chain of lymph-nodes in each groin, firm, movable, and discrete, varying in diameter from 1 to 2.5 cm. His extremities, skin, and reflexes were normal.

During the following six days his temperature varied between 98° and 99° F., the pulse between 80 and 90, and the respirations between 20 and 24. Blood-pressure was repeatedly as at entry. The itching persisted. Examination of the blood showed 9,200 white blood-cells with a differential count of 78 per cent. polymorphonuclear leukocytes, 20 per cent. lymphocytes, and 2 per

cent. monocytes. The hemoglobin content was 72 per cent. (Sahli). The red blood-cells showed moderate achromia; frequently red cells with stippling were seen. The platelets were normal. The Kahn test of the blood was negative. The icteric index of the blood-serum was 50. The clotting time was twelve minutes, with normal clot retraction in thirty minutes. The stools were clay colored and formed. No gross mucus, blood, or pus was seen. The guaiac reaction was strongly positive. Daily

Fig. 144.—*x*-Ray picture of the liver and gall-bladder area of Case I. The scattered small white shadows correspond to the calcified tubercles.

examination of the urine showed normal findings except for bile present.

Although the age, the painless jaundice, and the strongly guaiac test suggested malignancy as the most probable diagnosis, the absent of loss of weight and the suddenly increasing jaundice made us suspicious of mechanical obstruction of the common duct. In the presence of the severe obstructive jaundice, administration of tetra-iodophenolphthalein for visualization

of the gall-bladder seemed to be contraindicated. A direct gall-bladder plate was taken therefore. This *x*-ray plate showed a very unusual finding as seen in Fig. 144. There were numerous opaque shadows in the region of the liver which were interpreted as hepatic stones.

As the intensity of the jaundice increased rapidly there was no opportunity for further *x*-ray studies. Surgical consultation was held and immediate operation was advised.

Preoperative diagnosis: Mechanical non-malignant obstruction of the common duct, perhaps stone (?).

On September 22, 1926, the operation was performed by Dr. R. C. Cochrane. Incision was made in the upper right quadrant. Right rectus muscle split and retracted. Peritoneum incised. No free fluid found. Gall-bladder was found to be markedly distended and could not be emptied on pressure. Along the common duct were found numerous calcified glands about the size of a pea. On the surface of the liver were numerous small, yellowish, calcified nodules. Similar small nodes appeared over the peritoneum. The common duct was markedly dilated, and when incised, for the insertion of a T tube contained clear colorless viscid fluid. Calcified nodes along the common duct and one from the liver were removed. Rubber dam drain was inserted down the neck of the gall-bladder, and abdomen was closed in layers around the tube and drain. A dry sterile dressing was applied and the patient was sent to the ward in good condition. The pathologic diagnosis after gross and microscopic examination of the nodes, by Dr. E. B. Mallory, was healed calcified tuberculotic nodules.

For one week the patient drained bile through the wound, which then closed. The yellow color of the skin and scleræ disappeared gradually. There was a corresponding gradual reduction in the icteric index and an increase in the color of the stools. Further *x*-ray examination revealed scattered small shadows throughout the upper part of the peritoneum (Fig. 145). There was no evidence of tuberculosis of the lungs or pelvis (Figs. 146, 147), but a fused and compressed lumbar spine indicated an old healed tuberculosis of the spine (Fig. 145). The pa-

tient was discharged in good condition with the diagnosis of healed calcified disseminated tuberculosis of the peritoneum and liver. Obstruction of the common duct from outside by calcified periportal nodes. Hydrops of the gall-bladder.

Chronic lead poisoning.

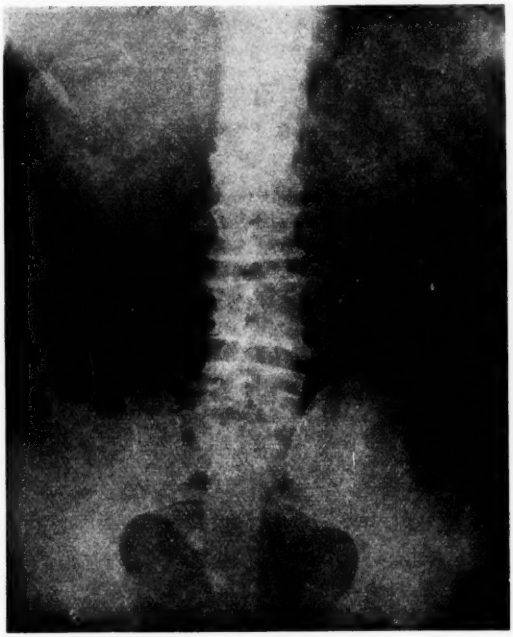

Fig. 145.—*x*-Ray picture of the abdominal region of Case I. There are scattered small white shadows throughout both sides of the upper aspect of the abdomen. The third and fourth lumbar vertebræ are fused.

He was thereafter followed in the Out-patient Department of the hospital.

Comment.—1. This patient is very unusual both from the point of view of clinical course and pathologic findings. In searching the literature I was unable to find a similar condition. Miliary tuberculosis of the liver is a relatively rare condition and is usually fatal. Miliary tuberculosis of the liver is not

ordinarily associated with jaundice. The only patient in the literature, reported by Dr. Thayer of Baltimore, had an intrahepatic process extensive enough to obstruct a sufficient number of bile-ducts to produce jaundice. A careful examination of the autopsy report of this patient, however, does not allow one to rule out mechanical obstruction of the common duct due to the presence of large periportal lymph-nodes.

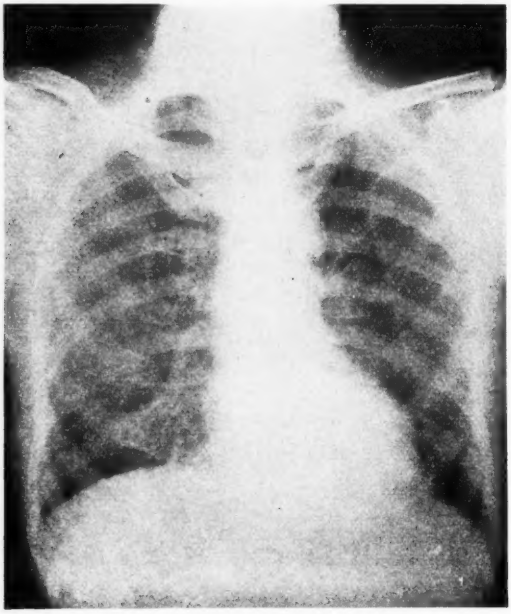

Fig. 146.—*x*-Ray picture of the lungs of Case I. There is no evidence of tuberculosis.

2. It is unusual, that although this patient has had a healed tuberculous process in the lumbar vertebræ and in the peritoneum and liver, very careful search failed to disclose any history related to the disease. Perhaps the acute process occurred in early childhood. It will be recalled that the lungs were free of tuberculosis.

3. Although there was a complete occlusion of the common duct, pain was absent. Occlusion of the common duct from outside, in contrast to occlusion from inside (stone, malignancy of the duct, stricture), is apt to be associated with painless jaundice, and it is noteworthy that the gastro-intestinal symptoms are not, as a rule, prominent. As distention of the gall-bladder is most marked when there is pressure due to malignancy, and, as in these patients, pain is often absent, it is very

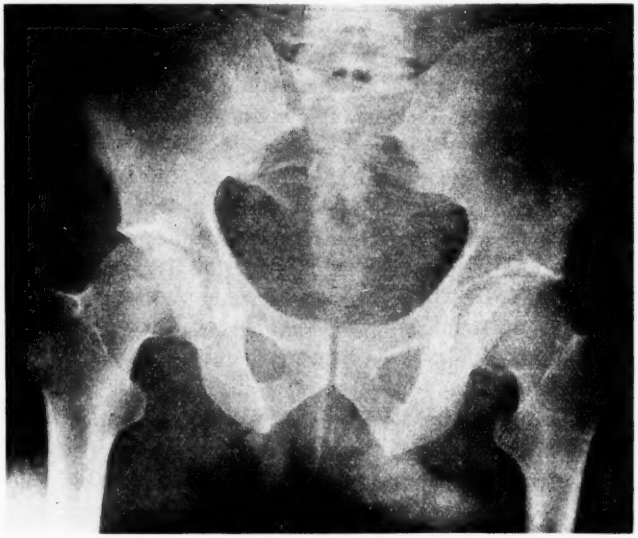

Fig. 147.—*x*-Ray picture of the pelvis of Case I. There is no evidence of tuberculosis.

suggestive that in the etiology of pain in "gall-bladder attack" the spasm of the ducts is the most important factor and distention of the wall of the gall-bladder, especially if it occurs gradually, is of little or no importance.

4. This patient complained of loss of strength, without loss of weight and he stated that the itching appeared before the jaundice. At the present time we believe that itching in connection with biliary disorders is due to retention of bile-salts,

although this point is far from being settled. There is no necessary relation between the retention of bile-salts and the bile-pigments. Bile-salts may be retained with normal bile-pigment excretion (dissociated jaundice). We observed a patient not long ago, who was suffering from intolerable itching and later developed symptoms of severe intoxication, in every respect resembling those of cholemia. The patient died and autopsy revealed a large liver with marked fatty degeneration and early alcoholic cirrhosis (Mallory). At no time did this patient show jaundice or other evidence of bile-pigment metabolism.

Clinically there is no relation between itching and intensity of jaundice. Itching may be the first signal of the beginning of severe disturbances of liver metabolism. Itching may subside when the jaundice appears. In other patients with complete occlusion of the common duct, itching may appear only with deep jaundice. I have repeatedly observed patients who died from cholemia without ever having had itching. There is perhaps a certain detoxicating capacity of the liver cells which if present, prevents the effect of the bile-salts on the skin. even in the presence of complete obstruction, which, however, if absent, will result in itching even if the bile-pigment elimination is normal.

5. Many observers were unable to feel this patient's gall-bladder. The case was an obscure one and the first *x*-ray picture suggested stones. The absence of a palpable gall-bladder should therefore support the diagnosis of stone in the common duct. It is true that upon operation a large distended gall-bladder was revealed, and therefore theoretically the condition behaved according to Courvoisier's law. Practically, however, Courvoisier's law was misleading in this patient. It was mentioned above that Courvoisier's law is especially apt to fail in cases with obscure clinical manifestations.

Case II.—Large Stones in the Common Duct Probably for Nine Months. Spontaneous Passage of the Stone Through the Intestines. Observation on Functional Pathology of the Stomach Due to Common Duct Obstruction. Periodic Acute

Dilatation of the Stomach as Reflex Disturbance from the Common Duct.—The next patient, a physician of fifty-five years, was admitted to the Thorndike Ward of the Boston City Hospital on February 3, 1926. The chief complaint was severe generalized abdominal pain.

His past history is unessential. Three years ago he had an attack of moderate upper abdominal pain without accompanying jaundice. This attack was diagnosed as due to gall-bladder disease. One year ago a similar but milder attack occurred, lasting a few hours only. With both of these attacks there was some slight tenderness in the right upper quadrant, and for the past year he has been "slightly tender there."

Two hours before his first admission the patient complained of slight distress in the abdomen and felt as if he were distended. From this time on the pain became increasingly severe, worse in the upper abdomen. He vomited once. There was slight spasm and tenderness in the right upper quadrant, but no icterus was observed. The rest of the physical examination was normal.

Soon after admission morphin sulphate gr. $\frac{1}{4}$ was given subcutaneously, with relief of the pain. Two hours after the pain had subsided, patient had a severe chill with a rise of temperature to 99.6° F. which later reached 102.2° F. About eight hours after entry slight icteric tint of the scleræ appeared. The first specimen of urine after the attack contained an increased amount of bile. The stools were formed, grayish-brown, guaiac test was negative, and bile was present. The microscopic examination was negative. The white blood-cell count was 10,800.

The next day the patient felt comfortable. The skin was yellow. The urine contained bile. The white blood-cell count was 8200 with polymorphonuclears 90 per cent., lymphocytes 7 per cent., monocytes 2 per cent., eosinophils 1 per cent. Hemoglobin was 85 per cent. (Newcomer). Serum bilirubin was 2.09 mgm. On February 5, 1926 the patient was still slightly jaundiced. The white blood-cell count was 4800, serum bilirubin 1.38. The stools were light gray, fat increased, soaps much increased. No gall-stones were recovered. On February 9, 1926, twelve hours following the intravenous injection of 3.1

grams of tetra-iodophenolphthalein, was given in 300 c.c. of salt solution over fifteen minutes. The gall-bladder filled well and after a fat meal emptied normally. The urine was normal, and the serum bilirubin content was 0.54 mgm.

In view of the clinical improvement and negative *x*-ray findings, operation was not advised and the patient left the hospital. The diagnosis at the time of discharge was chronic cholelithiasis.

About one week later the patient developed an attack similar to that described above. The jaundice was intense. Surgical consulatation was called and operation advised. At operation the gall-bladder was thickened and contained small stones. The gall-bladder was removed and the common duct drained. Following operation for eight weeks the patient drained large amounts of bile through the wound, and the stools were persistently clay colored.

In view of the attacks of pain, vomiting, occasional chill and fever, stone in the common duct was suspected and a second operation advised.

The operation was performed May 16, 1926. On opening the abdomen extensive adhesions were found about the former site of the gall-bladder. The common duct was exposed and opened. Three small soft stones about 1 to 2 mm. in diameter were removed, and the duct probed toward the duodenum. A small rubber catheter was inserted in the common duct. The abdomen was then closed in layers. Within two weeks following operation the wound healed and the patient left the hospital May 30, 1926, improved as far as his local condition was concerned. However, following the second operation the weakness continued, and he now suffered from painful joints. The fingers of both hands were swollen and occasionally they were red and tender on pressure.

About ten weeks following his discharge from the hospital one afternoon the patient experienced vague discomfort over the upper epigastrium which increased gradually to a dull pain. With the increase of pain which radiated to the epigastrium, there was marked tenderness on pressure over the epigastrium. The abdomen was prominent, bulging, and tense. The respira-

tory movement increased the epigastric pain. Patient felt nauseated. Several hours after the onset of the attack he asked for medical advice, and after the administration of $\frac{1}{4}$ gr. morphin sulphate subcutaneously he was promptly relieved. Next morning the sclera were slightly jaundiced, the urine was dark brown, and the stool gray in color. Within twenty-four hours, however, the skin, urine, and stools became normal in color.

During the following four months attacks of about the same nature occurred, on an average of every three to four days. These attacks disabled the patient almost completely. It is of special interest that nearly all of the attacks occurred in the late afternoon or during the night; they never were experienced in the forenoon. They were preceded by physical fatigue and emotional distress. The patient apparently became conscious, as the attacks recurred, of his own gastric peristalsis to such an extent that he could foretell the occurrence of an attack before any pain was experienced, by noting the cessation of the normal gastric movements. With the abolition of peristalsis there was an increasing distention of the stomach and an increase of pain. This pain was dull and quite different in nature from that experienced before the first and second operations. The pain usually radiated to the back, often to the right or left. There was nausea, and at times vomiting, during the attack. The severity of the attack depended on the degree of distention of the upper abdomen. If the patient took by mouth $\frac{1}{2}$ gr. codein or $\frac{1}{4}$ gr. morphin sulphate, the pain was promptly relieved. The relief occurred at once and was accompanied by the sensation of the beginning peristaltic movements.

The history of these attacks was corroborated by observations on the patient while in an attack. With the disappearance of peristaltic sounds over the stomach area, there followed an increasing distention of the abdomen over the stomach area. This area was tympanitic and rather tense, also very tender on palpation. Pain and nausea were increased by palpating the tympanitic area. Percussion showed that the left side of the diaphragm was pushed upward about two costal spaces. Fre-

quently there was spasm of the upper part of the right rectus muscle. Following the administration of ½ gr. codein, the patient complained of a sensation of slight mental excitement for about ten minutes, and after about fifteen to twenty minutes of great pain, he was *suddenly* relieved. At the same time peristalsis reappeared, the abdomen became soft, and the area of tympany decreased or disappeared. During the entire course the patient was not observed to swallow or belch gas.

If morphin or codein was not administered early in the attack the patient's scleræ were yellow the next morning, a condition which he could foretell with amazing accuracy from the duration of the attacks. After each attack the stools were light in color and the urine was dark. On a few occasions the attack was spontaneously relieved by vomiting. Repeated examination of the blood failed to reveal leukocytosis.

In view of the previous history of the patient and the nature of the peristent attacks, various opinions were expressed as to the cause of the attacks. It was thought that the patient might have a stone in the common duct which acted as a ball valve in the ampulla. The possibility of hepatic stones or temporary common duct occlusion due to adhesions, or perhaps to postoperative stricture, was considered by others. Operation was not advised as this was considered as jeopardizing the patient's life, and was left as a possible resort when the diagnosis became more definitely established.

In order to clarify the nature of the disease the patient was admitted to the hospital for observation on November 3, 1926. Except that the skin was of a suggestive light bronze color, the physical examination was negative. During the following twenty days the patient was in bed. He had numerous attacks similar to those described above. While in bed and when the evening meal was omitted the patient was free from attacks for ten days —the longest period observed. All the attacks while in the hospital were of short duration, due to the oral administration of medication.

The laboratory findings were as follows: Repeated examination of the urine showed no abnormal findings. At no time did

we find sugar in the urine. The color of the stools was rather light brown. The benzidine test was repeatedly negative.

The duodenal contents showed clear bile of normal color and viscosity. The sediment showed very rare white blood-cell, bile-stained, and rare cholesterin, and bile-pigment crystals interpreted as no evidence of infection. The ferments as tested by Dr. C. M. Jones of the Massachusetts General Hospital were all rather low, that for fat producing fatty acid to the extent of 0.88 c.c. of 1/10 normal NaOH (lower limits of normal 0.75); for protein 0.27 mgm. per 100 c.c. (lower limits of normal 0.75); for starch 0.9 mgm. per 100 c.c. (lower limits of normal 1).

The red blood-cell count under special diet increased from 3.8 millions to 5.4 per 1 cmm. The hemoglobin rose from 66 to 95 per cent. (Newcomer's method). The leukocyte count varied from 4800 to 7900. The differential white cell count showed polymorphonuclear leukocytes 44 to 77 per cent. Lymphocytes 10 to 23 per cent. Monocytes 2 to 22 per cent. Eosinophils varied between 0 to 5.5 per cent. Examination of numerous blood-smears showed the red cells normal in size, shape, and color. The blood-platelets seemed to be increased. The percentage of the reticulated cells was 0.7. The color index was .94. The non-protein-nitrogen was 26.9 mm., the blood-sugar 110 mgm. per 100 c.c. of blood. Icteric index was repeatedly found to be within normal limits.

The gastric secretion showed on four occasions no free hydrochloric acid before and after the test-meal. The combined hydrochloric acid varied from 4 to 13 c.c. of 1/10 normal hydrochloric acid.

Four *x*-ray examinations of the gastro-intestinal tract showed a persistent irregular filling defect of the pyloric region of the stomach. Although the two operations ruled out the possibility of malignancy and led to the suggestion that adhesions might be present, the findings caused uneasiness. It was thought that perhaps the filling defect was present because of reflex spasm of the musculature, due to adhesions and lack of peristalsis of sufficient intensity to fill out the defect. To differentiate between these two important possibilities, gr. 1/60 physostigmin was

injected. Fluoroscopic observation showed intense peristalsis five to seven minutes after administration of the drug. Ten minutes after the injection the filling defect disappeared for the first time in repeated observations within three months. The patient was also observed under the fluoroscope during several of his attacks. One of these observations, which it may be instructive to mention here, may thus be summarized. The patient complained at 4.00 A. M. of gradually increasing pain as described above. One hour later the epigastrium was moderately distended, with a large area of tympany and a high-pitched note on percussion. No peristaltic sound was heard. Spasm of the right rectus muscle was present. Although the patient was nauseated at 5.30 A. M., he drank two glasses of barium mixture. Fluoroscopic examination showed a large stomach, with no peristalsis. Shortly after that the nasuea became more intense, the patient vomited and the pain was relieved at once. Within the next five minutes he again swallowed two glasses of barium mixture and at this time the stomach was small, the area of gas less and peristalsis was very active. The barium, which before the relief of pain was stagnating in the stomach, passed readily through the pylorus and the rate of stomach emptying seemed normal.

Since the clinical observations, as well as the fluoroscopic examination (described later) indicated a close relationship between the attack of pain and gastric peristalsis, we attempted next to throw light on the question as to whether the changes in the movements of the stomach were primary or secondary. It was interesting to find out what the effect of induced peristalsis and increase of tone would have on the attack. For this reason physostigmin salicylate in doses 1/100 to 1/40 gr. was administered subcutaneously three times, and it was found that the attacks were relieved within ten to twenty minutes. As the most outstanding effect of the physostigmin observed under the fluoroscope was to increase gastric peristalsis and tone, it seemed possible that these changes might have an antagonistic effect on the common duct. (As we do not know, at present, of the direct action of physostigmin on the common duct, this latter possibility cannot be ruled out.)

Early in the evening of December 6th the patient developed a rather severe attack which could be relieved only by the administration of $\frac{1}{4}$ gr. of morphin. During the following two days there were three severe attacks. The morning after each attack the urine contained bile. There were no chills or fever present.

At 1.00 P. M. on December 10, 1926, the patient experienced vague abdominal pains with nausea, which increased in severity, so that at 5.00 P. M. $\frac{1}{4}$ gr. of morphin was administered, without relief. There was marked tenderness over the upper abdomen with spasm of the upper part of the right rectus. The pain was intolerable and came in spasms, radiating to the back. At 9.00 P. M. a second dose was given, and at 11.00 P. M. a third dose of $\frac{1}{4}$ gr. of morphin, with 1/100 gr. of atropin, without effect. The patient was pale, his pulse rapid, and he appeared to be in shock and vomited repeatedly. At 12.00 midnight 4 gr. of luminal was given by rectum, after which the pain gradually subsided within thirty minutes. At 2.00 A. M. severe chill lasting for one-half hour came on. The abdomen was now soft except for tenderness just below the xyphoid process.

The following morning found the patient comfortable, his skin and scleræ were jaundiced and the urine contained a large amount of bile. His temperature was 101° F., and the white blood count was 13,000.

A surgical consultation was held, and operation for common duct stone was advised.

On the next day the patient passed a clay-colored stool, in which a stone 10 x 7 mm. was found. Cross-section of the stone revealed a black nucleus, similar to the stones found in the gall-bladder, and a surrounding shell of $\frac{1}{2}$ mm. thickness which was light brownish yellow in color. Second and third stools passed were clay-colored. Urine contained bile up to two days after the attack. Tenderness on deep palpation of the abdomen persisted for four or five days following the passage of the stone. After that the patient felt comfortable, ate a regular diet, and gained 10 pounds within four weeks.

Comment.—1. At the time of the first operation for cholecystectomy this patient probably had four stones in the common

duct. It is a curious and not very rare clinical observation that a patient, who is free from gall-stone attacks for years, may suddenly pass multiple stones into the common duct. Gall-stones in the gall-bladder, as is well known, may be silent for years; but if they should become loose, and the compact arrangement be disturbed, they may cause a series of attacks.

2. This patient was suffering from the effect of a stone in the lower portion of the common duct. It is of interest to note that in the prevention or precipitation of the attacks mechanical factors, namely, exertion, walk, automobile ride, as well as emotional factors, played an important rôle.

3. Although *x*-ray examination of the gall-bladder after the injection of tetra-iodophenolphthalein revealed no filling defect, the subsequent operation revealed numerous small stones in the gall-bladder. This finding illustrates again the caution necessary in the interpretation of laboratory methods.

4. The patient's behavior illustrates the close relationship between the common bile-duct pathology and secondary functional disturbance of the stomach. This relationship is evident not only from symptoms referable to the stomach, but also from functional disturbances observed clinically and by *x*-ray examination. With each "attack," which was probably associated with secondary persistent spasm of the ampulla, an acute dilatation of the stomach developed, due probably to a reflex disturbance caused by spasm of the common duct. This conception is supported by the observation that when a minimal amount of codein or morphin was given, and the spasm of the duct presumably relieved, there was also an immediate cessation of the dilatation of the stomach. This finding was the more surprising because the direct effect of morphin or codein would tend to increase the distention of the stomach. The indirect effect of morphin and of codein, through their action on the duct, counteracted the possible slight direct effect on the stomach. It is, however, also of interest that by primarily relieving the acute dilatation of the stomach and including peristalsis by means of physostigmin, the attack was similarly benefited. Thus by in-

ducing peristalsis and decreasing the size of the stomach, the spasm of the common duct was apparently released.

That artificially induced dilatation of the stomach, or neutralization of gastric acidity of the stomach produces spasm of the sphincter muscle of Oddi in animals, was recently demonstrated by W. H. Cole. The observations on this patient would indicate that a similar reversible reflex relation may exist between the sphincter of Oddi and the stomach. Indeed, it must be considered more than a coincidence that this patient showed persistent achylia. As a matter of fact, all the 3 patients with obstruction within the common duct on whom analysis of the stomach content was made, showed achylia. This would indicate again a close reflex connection between the sphincter of Oddi and the functional activity of the stomach. This close reflex connection would also explain why fatigue, nervousness, or sleep which slows down gastric activity and secretion predisposes to "gall-stone attack," or, in other words, to spasm of the sphincter of Oddi.

The nature of these reflex connections between the lower portion of the common duct and the stomach is at present obscure. However, as vomiting is one of the most frequent signs of spasm of the common duct, and, since it has recently been shown vomiting is always a medullary reflex, it is suggestive that other functional disturbances of the stomach, associated with spasm of the common duct, may be due to highly developed medullary reflex disturbances.

5. Although this patient probably had the stone for nine months in the common duct, it was passed spontaneously, just at the time when a third surgical interference was contemplated. It is fair to state that considering the severity of a third surgical operation, the patient's life was perhaps saved by the conservative treatment followed. It is therefore worth while to remember that even such a large stone as found in the feces of the patient may pass spontaneously as late as nine months after lodging in the common duct. Whether the stone passed through the sphincter, or whether it tore into the intestine indirectly, cannot be stated with certainty. The fact that after its passage there was

no leukocytosis, fever, or evidences of peritoneal irritation, suggests that the stone entered the intestine through the opening of the common duct.

May I mention here that there are very few procedures which are as simple and often gratifying as the search for gall-stones in the stools, and at the same time there are few procedures that are so often wholly neglected. If physicians would take care to search for stones in the stools after an "attack of gall-stones," we would probably find that the passage of stones through the common duct occurs more often than we suspect.

6. The patient did not show the clinical intermittent hepatic fever of Charcot.

7. The numerous observations that the patient was jaundiced only following a prolonged attack, and the fact that the attacks could be stopped with surprisingly small doses of codein or morphin, drugs which could have had but one effect—the peripheral relaxation of the smooth muscles—suggest that during a so-called gall-stone attack the mechanical obstruction of the bile flow depends in part upon the intensity of the spasm of the lower portion of the common duct. Clinical observations indicate that the lower portion of the common duct is capable of long persisting spasm with considerable narrowing of the lumen or opening.

Case III.—Symptomless Jaundice at the Age of Seventy-two. Patient Entered Hospital with Cholemia. Autopsy Revealed Stone in the Dilated Common Duct with Abscesses in the Liver.—This patient is presented briefly because of the contrast to patient II, in that he shows the opposite extreme in the clinical behavior of stones in the common duct.

E. G., aged seventy-two, an American laborer, entered the Bellevue Hospital, New York City, on August 19, 1923. He was alternately comatose and irrational at the time of entry, and the history was obtained from the family with whom the patient was living. They stated that except for slight weakness during the past two or three months the patient had been in good health up until four weeks prior to entry, when he noticed gradually

increasing jaundice. He had vomited occasionally during the past two or three weeks. During the last one or two weeks the patient became irrational. He complained of no pain at any time. He felt no fever and had no chills.

Examination showed a white man of seventy to eighty, fairly well developed and nourished, who was alternately irrational and comatose. The skin and scleræ showed unusually deep jaundice with a tinge of olive-green color. Posteriorly over the lower part of the left side of the chest there was dulness and tubular breathing. The abdomen was soft, and not tender. Over the left upper quadrant, near the midline, a mass was vaguely palpated. This mass extended $2\frac{1}{2}$ inches below the costal margin. The rest of the physical examination was normal. The blood-pressure was 124/64 mm. Temperature was 96° to 97° F., except just before death, when it rose to 99° F. The pulse rate was 60 to 80. The stools were clay-colored, and the urine contained large amounts of bile. The rest of the findings were unessential. The patient's condition became gradually worse and he died August 23, 1923.

In view of the age, absence of symptoms, and suggestive mass in the epigastrium, the conditions was diagnosed as malignancy of the stomach or of the pancreas.

An autopsy was performed on August 23d. The body was that of a well-developed and fairly well-nourished white adult who appeared to be about seventy years old. There was marked jaundice over the entire body. The lower lobe of the left lung showed patchy consolidation. The heart was normal except for athermatous plaques over the walls of the coronary arteries. The spleen was twice as large as normal. The liver was only about half the normal size, and was removed from the body with difficulty due to numerous adhesions to the diaphragm and other surrounding tissues. The capsule was thickened and had a shaggy appearance. The gall-bladder could not be made out as such, but section of the liver revealed an atrophied, shrunken gall-bladder with thickened walls, yellowish-white on section, and an almost completely obliterated cavity. No stone was present. Section of the liver revealed five or six pea-sized ab-

scesses exuding greenish-yellow pus. Otherwise the cut surface was greenish-yellow in color, of increased consistency, with evidence of only slight increase in fibrous tissue. On opening the common duct from the duodenum, about 2 cm. proximal to the sphincter, there was revealed a large stone about $1\frac{1}{2}$ cm. in diameter which completely occluded the duct. Behind the point of lodgment of the stone the common duct was dilated to the size of the little finger.

Comment.—1. While patient II exhibited numerous symptoms and signs as a result of stone in the common duct, this patient developed severe cholemia practically symptomless. It is for this reason that he did not seek medical advice, and when he entered the hospital he was in a hopeless condition. It is of course questionable whether his condition would have been properly diagnosed had he entered the hospital earlier. We are apt to forget, as we indeed did, that stone in the common duct may occasionally cause very few symptoms, and we are inclined to diagnose malignancy or cirrhosis after the age of forty with symptomless jaundice. This patient's fate should teach us again that the diagnosis of stone can be ruled out only if there is direct evidence for malignancy or other definite obstructive disease. The fact that the common duct was markedly dilated and that there were abscesses in the liver and firm adhesions surrounding the common duct indicates that the stone had been present in the common duct for a considerable length of time.

2. Abscesses in the liver are one of the complications following the partial stagnation of bile in the common duct. Purulent cholangitis with or without strictures at various parts of the biliary systems, and subacute or chronic interstitial pancreatitis, may follow a long stay of a stone in the common duct.

3. Painless jaundice without direct clinical evidence of malignancy, cirrhosis of the liver, or infection should make us suspect benign mechanical obstruction of the common bile-duct, and if we cannot arrive at a definite clinical conclusion, laparotomy is always justified.

Case IV.—Obstruction of the Common Bile-duct by a Small Carcinoma of the Ampulla of Vater Without Metastasis, Revealed Only on Microscopic Examination. Marked Secondary Anemia and Achylia Gastrica.—P. B., a Belgian housewife of forty-seven years, entered the Fourth Medical Division of the Boston City Hospital March 4, 1926. Her chief complaints were weakness and jaundice.

Until last June, seven months ago, this patient had always been fairly well, but never strong. In July she suddenly fainted, after having felt unusually weak for a short time. Following this incident she continued to feel weak, but was not confined to bed constantly. Her skin became yellow, and food did not agree with her. The yellowness disappeared some time in August and she felt better. Her stools were not unusual in color at this time, there was no itching, and her tongue was not sore, fissured, smooth or reddened, so far as she knows. The indigestion was characterized by gaseous eructations, nausea, and frequent vomiting of recently taken food within thirty to sixty minutes after eating. There was no pain, fever, or chill.

From the time the jaundice disappeared in August, until about December 1st, she was in her usual state of health and activity, but after December 1st she again was yellow, very weak, and often nauseated. She vomited frequently but irregularly. Her feet tingled and itched, especially on the soles, and she felt sick enough to remain in bed for the three months. Her urine was of a dark "rum color." Until two weeks ago she did not pass any light-colored or unusual stools; in the past two weeks, however, the stools have been "white" or light yellow. There was never diarrhea, and she never went more than four days without a movement.

For two months she was aware of a dull aching pain, in the right back beneath the scapula nearer its vertebral border, not enough, however, to prevent sleep or waken her. During this time she has also had a few short, not severe, chills, followed by a feeling of warmth. Twenty-four hours before entry the patient had her first attack of severe pain. It was constant, "boring," and severe enough to cause her to cry out, double up, and

"yell." It appeared first in the right back about the spine of the scapula, and radiated over the shoulder and thorax to the epigastrium and thence to the suprapubic region. It lasted about two hours, and for three-quarters of an hour she was "unconscious." The pain disappeared after the evacuation of what seemed to have been an unusually large amount of very foul-smelling feces. A sensation of being cold all over followed. The patient's family, marital, social, and past history is unessential and does not bear on her present condition.

Physical examination showed the patient to be prone in bed, not uncomfortable, and alert. Her development was just under average with apparently some loss of weight, and her skin was yellow, sclera less yellow. Her lips and the tissue beneath the finger-nails were very pale. Face was pale, rather blank and expressionless, even during conversation. The abdomen was well developed and symmetric. There was a smooth, non-tender mass in the right hypochondrium, coming apparently from beneath the costal margin. It seemed to have a sharp edge and to move with respiration. The rest of the physical examination revealed no abnormal findings.

The urine contained bile and the stools were grayish in color, without gross blood or mucus; the guaiac test was strongly positive on repeated examination. Gastric analysis showed no free hydrochloric acid, and a positive guaiac test. Examination of the blood showed a red blood-cell count of 1,864,000 to 2,648,000, and a hemoglobin of 23 to 25 per cent. (Sahli). Repeated white blood-cell counts showed 13,700 to 17,340 white cells, with 79 per cent. polymorphonuclear leukocytes. Blood-smears showed marked achromia of the red blood-cells, poikilocytosis, no anisocytosis. Platelets were increased. Reticulated cells 0.5 per cent. Blood Wassermann negative. An *x*-ray plate of the gall-bladder area revealed a shadow which was interpreted as a large gall-bladder.

While in the hospital the patient continued to lose in strength. The temperature, pulse, and respirations were within normal limits. Considering the history, the severe secondary anemia, the mass below the right costal margin, with more over moderate

cholemia, light colored stools and a positive guaiac reaction, the condition was diagnosed as malignant tumor of the gall-bladder or the stomach, and laparotomy was advised.

The operation was performed by Dr. Hubbard on March 10, 1926. On opening the peritoneum no free fluid was found. The gall-bladder was enlarged with thickened wall, and emptied on pressure. It was removed, and the wound closed. The post-operative diagnosis was chronic cholecystitis. Following operation and transfusion the patient developed a slight fever, 98° to 100.5° F., her pulse rate was about 100, she continued to fail slowly, and died on March 17, 1926.

A postmortem examination of the body was performed next day by Dr. C. L. Swan. The body was deeply jaundiced. The peritoneal cavity contained about 200 c.c. bile-stained fluid. The parietal peritoneum of the right upper quadrant was dull and covered with fibrin. The intestines were covered by omentum, bound together by fine fibrinous adhesions. On opening the duodenum bile was seen to exude from the ampulla, showing patency of the ducts. The duodenal mucosa, particularly at the site of the ampulla, was slightly thicker than normal, but no definite area of induration was felt. The rest of the examination was unessential.

The *anatomic diagnosis* was acute generalized peritonitis. Icterus.

Microscopic examination by Dr. F. B. Mallory was as follows: Sections through the duodenum at the level of the ampulla. Tumor composed of atypical columnar epithelial cells in gland formation. The glands were large and irregular with several layers of epithelium. Their lumina were filled with tumor giant cells and endothelial leukocytes. Numerous mitoses were present and the tumor infiltrated with polymorphonuclear leukocytes and lymphocytes. Part of the mucosa of the duodenum seen in the section was entirely replaced by rapidly growing tumor.

Comment.—1. The patient just presented was suffering from partial occlusion of the ampulla of Vater due to a carcinoma arising from the ampulla. The growth was so small that it was not recognized either by the surgeon or by the junior pathologist

at autopsy. Had it not been for Dr. Mallory's skill and experience the patient's condition would never have been diagnosed. On his advice special care was taken in the microscopic examination of the duodenum and ampulla, and the malignant growth was discovered.

As primary carcinoma of the ampulla of Vater is a rare condition, it may be useful to mention briefly certain characteristics of this tumor. I am not aware of the exact number of cases reported in the literature. Rolleston up to 1904 was able to collect 19 cases of undoubted carcinoma of the ampulla. Several cases reported in the literature as carcinoma of the ampulla are those of the terminal portion of the common bile-duct or the termination of Wirsung's duct. There are authors who attempt to separate from carcinomata of the ampulla those arising from the papilla duodeni (biliary papilla). The definite separation of this last mentioned carcinoma may frequently be very difficult. As far as the clinical behavior of the patients is concerned, the history and findings of the patient presented here are quite typical of what is generally observed in this condition.

The first symptoms which present themselves in patients suffering from carcinoma of the ampulla are usually jaundice and pain. It is interesting that similarly to the behavior of this patient the jaundice is apt to be intermittent, or at least fluctuating. The explanation of this phenomenon lies perhaps in the mechanical compensatory changes in the function of the common duct during the early part of the disease. The character of the pain was similar to that observed in the presence of stone. Similarly, intermittent hepatic fever may be present as with stone in the common duct. In this patient, however, such fever was not observed. Gastric symptoms are frequently observed. Secondary growth is rather rare, because the critical location of the original tumor is apt to cause severe interference with vital functions, before metastasis occurs.

The clinical diagnosis is difficult. In this patient it was not made. One should think of carcinoma of the large biliary tract if a patient suffering from "gall-stone colic" shows a large gall-

bladder, and if without direct evidence of malignancy he nevertheless fails rapidly. True "gall-stone colic" is usually associated with a small gall-bladder. And malignant tumors causing pressure on the common duct from the outside often do not cause pain, especially not if they are so small that they are not palpated. The rare combination, therefore, of "gall-stone" attack with large gall-bladder and loss of weight should make us suspicious of malignancy of the common duct. Surgical removal of the primary growth has repeatedly been attempted but with rare final recovery.

2. I should like to call attention again to the achylia. I suspect that this may be due to certain reflex disturbances between the ampulla and the stomach, as discussed above. The severe secondary anemia may be associated with the achylia.

Achylia gastrica and anemia, occasionally even of the primary type, has been observed in other patients in this hospital with gall-bladder and duct pathology.

Case V. Stricture of the Ampulla of Vater Caused Probably by Irritation of a Temporarily Lodged Stone. Marked Secondary Cystic Degeneration of the Pancreas with Diffuse Fibrosis Replacing the Glandular Tissue of the Pancreas. Relative Preservation of the Islands of Langerhans. No Evidence of Diabetes.—T. M., an American laborer of sixty-two years, was admitted to the Second Medical Division of the Bellevue Hospital of New York City on July 8, 1924.

On entrance the patient's chief complaints were great weakness, jaundice, and marked loss of weight.

About September, 1923 the patient noticed loss of strength and "feeling of weakness." The same symptoms increased gradually so that at the end of February, 1924, he was forced to give up his work. In December, 1924, he noticed that his skin was jaundiced. The jaundice persisted after that, though it showed definite fluctuation in intensity.

His appetite was poor during the last few months, and shortly before entry he vomited once or twice. Occasionally he experienced vague epigastric distress which was relieved by the

belching of gas. He had lost over 45 pounds in the past ten months. On admission he felt completely prostrated, unable to move on account of weakness, and his vision, was failing. During April, 1924, he was "stone deaf" for a short period. Recently he had been getting short of breath. He also had been having frequent attacks of diarrhea, with clay-colored stools and deeply colored urine. No melena, no sharp attacks of pain. No polyuria or polydipsia had been observed.

The patient was in the Post-Graduate Hospital from February 28, 1924 to March 14, 1924, The examination of the patient there showed an icteroid tint of the skin and sclera. The patient did not look acutely ill. The liver edge was felt three fingers below the costal margin in the anterior axillary line on the right side. It felt lobulated, but not nodular. There was no tenderness. The rest of the examination was unessential. Laparotomy was advised, which the patient refused.

When the patient entered the Bellevue Hospital he was markedly emaciated, and apparently very weak. He looked very ill and the jaundice was unusually marked.

The abdomen was flaccid. The liver edge was very firm and sharp and reached 5 cm. below the costal margin. No other mass was felt and there was no tenderness. There was pitting edema over the dorsum of the feet and of the ankles. *x*-Ray examination of the chest showed a difusely dilated aorta. Fluoroscopic examination of the stomach and duodenum showed no filling defect. The peristalsis was sluggish and the stomach emptied within six hours. Repeated examination of the stomach contents showed no free hydrochloric acid. The duodenal contents obtained was bile free. There was no amylolytic activity. Repeated examination of the urine showed normal findings except that bile was present. At no time was glucose present. The stools were negative for bile.

The blood-sugar was 110 to 136 mgm. per 100 c.c. on repeated examination. The blood chlorids were 476 mgm. per 100 c.c. The blood Wassermann was negative. The red blood-cell count was 4,436,000; hemoglobin content of the blood 78 per cent.;

white blood-cell count 11,400, with normal differential count. The coagulation time was six minutes, and the bleeding time five and a half minutes. Icteric index 166. Soon after admission patient became irrational, comatose, and died July 11, 1924. Considering the loss of weight and gradually increasing weakness and painless jaundice, the diagnosis of malignant tumor with the source probably in the pancreas was made.

A postmortem examination of the body was performed July 11, 1924. The findings which bear on the clinical condition of the patient are as follows:

The body was markedly emaciated. There was a deep yellow color of the skin. The coronary arteries of the heart were tortuous stiff, and calcified. The spleen was somewhat enlarged and soft. The intestinal contents were clay colored. There was no evidence of bile. The head of the pancreas was firm, but not enlarged. Cross-sections throughout the organ showed dilated ducts with numerous cystic areas containing clear fluid, some of the cysts being 1 to 2 cm. in diameter. The gall-bladder was dark in color and moderately distended. Bile could not be expressed into the duct. On opening there appeared dark fluid with a number of small stones. On opening the duodenum, bile was seen to exude from the papilla. This, however, was observed after a mass of firm adhesions around the portal area between liver, gall-bladder, and duodenum had been freed. These adhesions were considered the cause of the evident obstruction of the ampulla of Vater and of the cystic duct. No stone was found in the ampulla of Vater or elsewhere in the biliary tracts.

The liver was closely adherent to the diaphragm and to the stomach. It was dark green in color, enlarged, and of firm consistency. On section it had a mottled appearance. The Wirsung duct was markedly and the common duct only slightly dilated.

Microscopic examination of the pancreas showed in numerous sections an extensive fibrosis with infiltration of mononuclear cells. The fibrous tissue either completely replaced the glandular tissue of the pancreas, or produced marked atrophy of the

latter. Embedded within the connective tissue there were numerous islands of Langerhans present and intact. Some of these islands were rather large. Both the larger and smaller pancreatic ducts were dilated.

Comment.—1. The marked loss of weight and the weakness in this patient was due to the absence of pancreatic ferments. It is my experience that in common duct obstruction, partial or complete, the weakness experienced is much greater than that to be expected from the degree of jaundice present. Patients suffering from jaundice of equal intensity, caused by an intrahepatic process, for example, are less weak as a rule than if the jaundice is caused by common duct occlusion. In this patient, who showed marked pathology of the pancreas, pronounced weakness was experienced over three months before the onset of jaundice.

2. One should remember, therefore, that weakness and marked loss of weight in the presence of long persisting occlusion of the common duct is not necessarily in favor of malignancy. With correct diagnosis this patient's fate could not have been altered, but the lesson nevertheless is evident. In painless jaundice with loss of weight and strength, other conditions than malignant tumors should also be considered.

3. In view of the presence of stones in the gall-bladder, in view of the markedly dilated duct of Wirsung, it is fair to assume that this patient had had a stone in the ampulla for a long time. The patient eventually passed the stone, but the inflammatory process around the ampulla precipitated by the irritative effect of the stone continued, and the adhesions eventually produced a relative stricture of the opening of the common duct. Such a supposition is almost inevitable. That persisting stones may indeed produce firm adhesions around the duct was also observed in Case III. I have in a few instances observed dilated common ducts with partial or complete occlusions of the ampulla without the presence of stone in the common duct or ampulla at the time of postmortem examination. A patient with a similar condition was observed not long ago in the Boston City Hospital. I can offer no other explanation than the supposition that stone with

secondary inflammatory lesions along the duct may produce single or multiple strictures.

4. An unusually interesting feature in the clinical history of this patient was the lack of disturbance in the carbohydrate metabolism, as measured by the blood-sugar and glucose content of the urine, in the presence of such a marked and diffuse destructive process in the pancreas. This very surprising apparent discrepancy was explained, however, after microscopic examination of the pancreas, which showed a remarkable preservation of the island of Langerhans within the connective tissue. It became evident then that we were dealing with a beautiful clinical repetition of the clinical experiment of Ssobolew, who observed that after the ligation of the pancreatic duct the pancreatic tissue degenerates, but the islands of Langerhans persist and the animals do not develop diabetes.

Such findings as observed in this patient should stimulate us to careful analysis of clinical symptoms and signs, not only for the sake of diagnosis but also for the sake of the discovery of general correlations. How often the clinic can show correlations recognized long ago—which are only now beginning to be crudely reproduced by experiments in the laboratory!

I am indebted to Dr. Eugene F. DuBois and to Dr. Douglas Symmers for allowing me the publication of Cases III and V whom I observed in Bellevue Hospital, New York City.

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CLINIC OF DR. RAPHAEL ISAACS

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ANEMIA IN CANCER

THERE is a general impression among the laity that patients with cancer have anemia. While many individuals become anemic in the later stages of malignant disease, quite a number run their entire course with but little evidence of diminution of the circulating hemoglobin. Anemia develops usually when there is an actual blood loss, or when the blood-forming organs are invaded by neoplastic tissue. In some cases there appears to be a hemolytic anemia, classically found in cancer of the stomach and liver. In these conditions, the anemia is often out of proportion to other signs of the disease and may be of a type to simulate, in some respects, a primary anemia. When there is considerable hemorrhage, the characteristics of the blood are those of anemia due to blood loss. When the bone-marrow is the seat of extensive metastases, however, the blood-picture may simulate, in some respects, pernicious anemia. This happens in about one-half of the patients with metastatic carcinoma in the bones. When the lymphoblastomas involve the bone-marrow, the blood may show evidence of bone-marrow "irritation," with atypical and abortive young cells, or the marrow may become aplastic in the sense that production is reduced to a minimum.

Case I.—The first patient is a man of fifty-five, whose occupation is that of a laborer. A little over a year ago he noticed that he was becoming dyspneic on walking and climbing

up stairs. This became worse and eventually he had to stop work. He noted that he had swelling of both legs. This was more marked at night, but was practically gone in the morning. About six months ago he noticed that there was tingling and numbness in the toes. This has been progressive. At that time he noticed that he was quite yellow. The intensity of this yellowness varied so that at times it was hardly noticeable, but at other times it was quite obvious. A few weeks ago he noted a swelling in the upper part of his abdomen. This has apparently increased and decreased in size at various times. He has had no orthopnea, but has had slight palpitation during the present illness. There has been no pain. A year and a half ago he weighed 200 pounds, but now weighs 150 pounds. He does not consider that his general strength has been impaired, but he tires rather easily and has not been doing any hard work. His appetite is as good as ever. He eats three good meals a day and does not know of any foods that especially disagree with him. There is no history of gastric distress, although during the past months he has been troubled with gas. His bowels move regularly, but for the past ten months he has taken cathartics occasionally. There have been no clay-colored or tarry stools so far as he knows. Three weeks ago he says he passed a dark "blood clot."

The other features of his history are unimportant for the present consideration. There is no history of cancer in his family.

Physical Examination.—He is a well-developed but obviously emaciated white man, with grayish hair and with a sallow hue to the skin. There is no definite jaundice. His scleræ are not icteric. The general picture is that of cachexia. The tongue is not smooth. The reflexes are normal. There are no abnormally enlarged peripheral lymph-nodes.

The abdomen presents several interesting features. There is a definite bulge in the epigastrium, where there is a palpable mass extending 10 centimeters below the costal margin in the mid-line. The mass is firm, nodular, and moves slightly with respiration. The liver is palpable 8.5 centimeters below the costal margin. It is not tender and the edge is smooth. The

spleen is not palpable. There are no other masses, and there is no tenderness or rigidity. There are no bleeding hemorrhoids. There is marked pitting edema of the lower part of both of his legs.

In view of the mass and the history of passing blood, some form of malignant disease is to be suspected. The absence of a history of gastro-intestinal disturbance makes one wonder what organ is at fault. The Roentgen-ray studies of the gastro-intestinal tract showed a constant irregularity at the pyloric end of the stomach, and the stomach was definitely fixed in this region, which corresponds to the location of the palpable mass. The fluoroscopic examination suggested that his spleen was probably enlarged. The Roentgen rays revealed no other abnormalities.

The fasting stomach contents were 42 c.c., yellowish, and with a small fleck of red blood, presumably due to trauma. There was no free hydrochloric acid, and the total acid was equivalent to 3 c.c. of decinormal sodium hydroxid solution. Lactic acid was present in appreciable amount. The sediment showed numerous large rod-shaped bacilli, epithelial cells, and white blood-cells. No red blood-cells were seen. Forty-five minutes after a test-meal, 60 c.c. of substance were obtained. It was whitish and mixed with easily visible particles of bread. There was no blood present as told by the "guaiac test." There was no free hydrochloric acid. The total acid was equivalent to 7 c.c. of decinormal sodium hydroxid, and some lactic acid was present. The sediment was very much like that of the fasting gastric contents except that there were numerous starch grains present from the bread of the test-meal.

The urine at times showed a very slight trace of albumin, but otherwise showed no abnormalities.

A study of the blood brought out some interesting features. The first examination, about a year after the onset of the patient's symptoms, showed as follows:

White blood-cells, 9,650 per cu. mm.
Red blood-cells, 2,610,000 per cu. mm.
Hemoglobin, 25 per cent. (Sahli).
Color index, 0.5.

Differential count:

	Per cent.
Polymorphonuclear neutrophils	69.5
Polymorphonuclear eosinophils	3.0
Neutrophilic myelocytes	4.0
Small lymphocytes	12.5
Atypical lymphocytes	0.5
Monocytes	10.0
Atypical monocytes	0.5

There was a definite variation in the size of the red blood-cells. The diameter of about 89 per cent. of erythrocytes measured from 6 to 8 micra, 5 per cent. being smaller and 6 per cent. larger. The largest measured 10 micra in diameter. Many of them showed diffuse basophilia. A few of the cells were irregular in shape. Most of the corpuscles were hypochromic.

The platelets appeared greatly increased in number.

As the disease progressed the red blood-cell count remained essentially the same during the three following months. There was a slight drop in the percentage of hemoglobin so that the color index remained much less than 1. The icteric index of the blood-serum was 5. The blood Wassermann was negative.

At times examination of the stools gave a strongly positive test for occult blood, but at other times they yielded a negative test. No parasites or their eggs were found.

The features of this patient are, then, a definite lesion in the stomach that has all the clinical features of a malignant one, and progressive anemia. Before the diagnosis of carcinoma of the stomach was made, the patient presented some features suggestive of pernicious anemia. His symptoms and certain signs, of course, were those of any anemia; but his grayish hair, slightly yellow color of the skin, and absence of free hydrochloric acid in the gastric contents, would have made one wonder if he had pernicious anemia. He had no tongue or central nervous system lesions of this disease, however, The low color index, the relatively high percentage of polymorphonuclear leukocytes, the greatly increased number of platelets, relative infrequency of large red blood-cells and absence of extremely large ones, the presence of blood in the stools at times, and the normal icteric index, were more characteristic of secondary

anemia from chronic blood loss. The increased number of blood-platelets, the numerous red blood-cells showing diffuse basophilia, the relatively large percentage of bone-marrow cells, and the myelocytes were evidence of active changes in the bone-marrow in an effort to increase the production of blood-cells. The red blood-corpuscles themselves were apparently made faster than the supply of hemoglobin so that their content was about half the normal amount. This was shown by the low color index and the small amount of eosin which the red blood-cells absorbed when staining. This hypochromia in stained blood-films gives important data if correctly interpreted. The pallor of the center of the blood-cells is not the critical feature, but the amount of eosin which the hemoglobin of the cells has held, in proportion to the amount which it could have taken up, as evidenced by the depth of color of the red and purple staining elements of the white blood-corpuscles. The absence of free hydrochloric acid in the stomach could have been associated with severe anemia or carcinoma of the stomach. The important feature to note is that the bleeding was periodic. The blood loss must have extended over a long time because there was no leukocytosis of acute hemorrhage, but there must have been times during the day, or possibly days at a time, when no bleeding took place. The distinct increase in number of young red blood-cells as shown by the number of basophilic ones strongly suggests recent loss of blood, as does the great increase of blood-platelets. The importance of repeated stool examinations under these conditions is emphasized, using precautions, of course, to eliminate positive blood-tests from the food.

Certain features of this type of anemia in cancer are shown by the next case.

Case II.—This man, fifty years of age, has been troubled for over a year with epigastric pain and distress, vomiting, and loss of weight. The pain did not radiate but remained localized. It came at night, usually several hours after the evening meal. It has lasted usually several hours, and sometimes would not recur for days at a time. Constipation and gaseous eructations

have been troublesome features. After heavy meals he vomited at intervals of about three hours. There has been no diarrhea and no blood, as far as he knows, in the vomitus or in the stools. He has lost about 25 pounds in the last eight months.

Physical Examination.—He is a pale, somewhat emaciated man. The abdomen is flat, but there is a distinct sense of re-

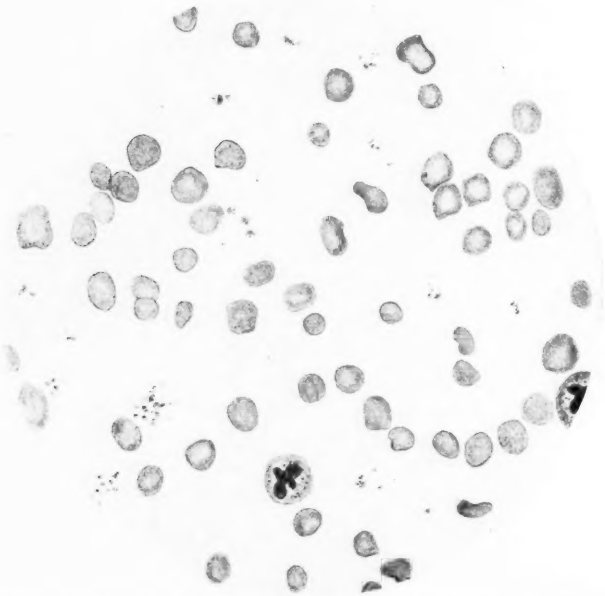

Fig. 148.—Blood film from Case II during period of anemia. The blood-platelets are increased in number. The red blood-cells show variation in the depth of staining, the young forms (basophilic) appearing darker. There is but slight variation in shape. No extremely large red cells are present. This blood shows some characteristics of an anemia from chronic blood loss.

sistance in the epigastrium extending to the left of the mid-line, giving the impression of an underlying mass. A mass can be felt here, which at times is more readily felt than at others. The liver dulness extends 2 cm. below the costal margin, but the liver and spleen are not palpable. The peripheral lymph-nodes are not enlarged.

After the disease had progressed for about a year, definite changes were demonstrated in the stomach by means of a Roentgen-ray examination. A large area in the lower part of the stomach was occupied by a definite irregular filling defect, which had the characteristic appearance of cancer of the stomach. The lesion appeared to involve at least the lower third of the stomach.

The red blood-cells at this time were 4,800,000 per cu. mm. There were 17,400 white blood-cells per cu. mm., and the hemoglobin was 55 per cent. (Sahli). As a palliative measure he was given Roentgen-ray treatments with the short wave-length *x*-ray over the abdominal tumor. Four treatments corresponding to an erythemal dose over the front and an erythemal dose over the back were administered.

During the three months following this there was a progressive anemia, the red blood-cell count dropping to 3,700,000 and later to 1,800,000 per cu. mm., the hemoglobin dropping to 48 per cent. and later to 23 per cent. The white blood-cells dropped to 9600, and later to 7200 per cu. mm. after another smaller Roentgen-ray treatment. The differential count was as follows:

	Per cent.
Polymorphonuclear neutrophils	73
Polymorphonuclear eosinophils	7
Polymorphonuclear basophils	1
Small lymphocytes	7
Large lymphocytes	1
Monocytes	10
Atypical cells	1

Of the red blood-cells, 97 per cent. measured from 6 to 8 micra, with only 3 per cent. larger than this, the largest measuring 10 micra. Most of the red blood-cells appeared fairly well colored, but there were some pale forms. Microcytes were very rare, and a deformed blood-cell was noted only occasionally. The blood-platelets were increased in numbers.

This blood is that of a secondary anemia. It has features to suggest chronic blood loss rather than abnormal blood destruction. The red blood-cells are mostly of the normal type, but

they have too little hemoglobin, as shown by the low color index. There has been a response on the part of the bone-marrow, and the increased number of blood-platelets and relative increase in the percentage of bone-marrow leukocytes show that the blood-cell production is active. The blood, as described above, may have shown some of the effects of a Roentgen-ray treatment given three weeks previous to the examination. The low percentage of lymphocytes and increased percentage of eosinophils may have been, in part, the result of this. Such changes, however, occur after hemorrhage, even when no irradiation has been given. An eosinophilia is seen in some patients with carcinoma of the stomach.

Another Roentgen-ray treatment was given at this time and during the following months the red blood-count rose. Two months later it had reached 4,200,000 per cu. mm. with 62 per cent. (Sahli) hemoglobin, and 12,600 white blood-cells per cu. mm. The hemoglobin and red blood-cell count remained at about this level during the next six months. The stools gave negative tests for blood on numerous occasions during this period.

The features presented by this case, then, are those of a temporary anemia probably related to several factors. First, the repeated vomiting and loss of nourishment may have been contributory, and it is highly probable that blood loss occurred although it was not detected. Second, the *x*-rays may have played a part. The temporary clinical improvement after the second course of Roentgen-ray treatments, and after a third course given later, makes one believe there was a good effect on the blood when either the activity of the tumor was checked or undetected bleeding ceased. The fact that no blood was found in the stools may mean that there was no bleeding, or it may mean that the bleeding appeared at times and disappeared at others, as in the previous patient. The man, then, presents a feature of cancer of the stomach with anemia which is often not recognized, namely, that anemia may lessen as time passes by although the patient approaches onward toward death.

Cancer of the stomach is peculiarly apt to produce a degree of anemia quite out of proportion to any of the other signs of

the disease. Indeed, other signs may be conspicuous by their absence, when the anemia is so profound that a diagnosis of pernicious anemia is not infrequently considered.

The next case, one of carcinoma of the breast with metastases to the bones, shows another feature of anemia in cancer.

Case III.—This patient is a woman fifty-four years of age. She has had a growth in her right breast for about a year. Several months ago she noted a feeling of lameness in her hip and back which became progressively worse.

Physical Examination.—She is an obese, gray-haired woman, very pale. The right breast shows a mass involving the nipple and infiltrating the upper outer quadrant. The nipple is replaced by an ulcerated area measuring about 2 cm. in diameter. Two enlarged lymph-nodes are palpable in the right axilla. There are no palpable lymph-nodes elsewhere. Roentgenogram studies of her spine, pelvis, and femurs show evidence of extensive metastatic malignancy. The ribs and clavicles are also involved.

The blood shows 10,700 white blood-cells per cu. mm., 1,350,000 red blood-cells, 32 per cent. (Sahli) hemoglobin. The differential count is as follows:

	Per cent.
Polymorphonuclear neutrophils	53
Small lymphocytes	25
Large lymphocytes	11
Atypical lymphocytes	7
Monocytes	4

Anisocytosis of the red blood-cells is marked, but there is only slight poikilocytosis. Some of the cells appear achromic, but not all. There are many diffusely basophilic red cells and a few nucleated red blood-cells. Sixty-seven per cent. of the red blood-corpuscles measure from 6 to 8 micra in diameter, while 33 per cent. are larger, 23 per cent. measuring 10 micra. The largest measure 11 micra. The platelets are decreased in number.

The blood Wassermann is negative.

The urine and stools show no evidence of abnormality.

This woman, then, shows carcinoma of the breast with metastases to the bone-marrow. There is marked anemia with a high color index (1.2−), a relatively low percentage of polymorphonuclear neutrophils, decrease in number of platelets,

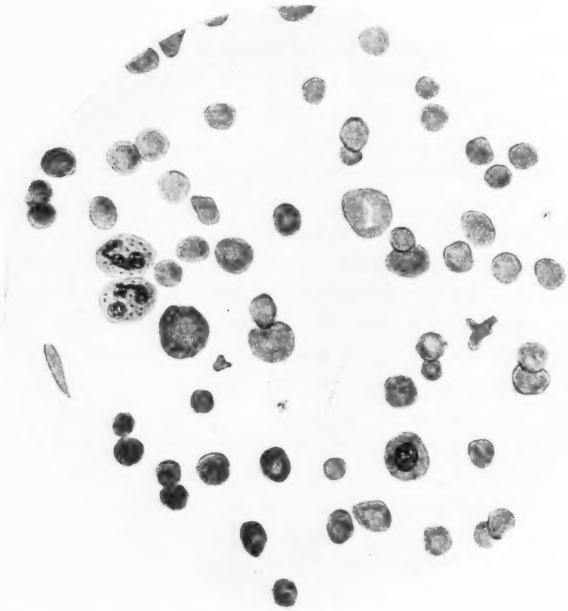

Fig. 149.—Blood film from Case III during period of anemia. A feature is the sparsity of blood-platelets. Numerous young (basophilic and more deeply stained) red blood-cells are present, and one nucleated red cell appears in this field. A few abnormally shaped red blood-cells are present. The variation in the size of the red blood-cells is marked and both microcytes and macrocytes are present in the film. This blood shows some of the characteristic features of metastatic invasion of the bone-marrow by tumor tissue.

increase in number of large red blood-cells, and some of the malformations of red blood-cells seen in pernicious anemia. She did not have the smooth tongue which frequently occurs in that disease. The most of her subjective symptoms were those of any severe anemia.

The blood-picture of "metastatic anemia," as this is sometimes called, frequently differs from that of typical pernicious anemia in certain respects. There is usually an increased white blood-cell count, although it is not always present. A more common condition in "metastatic anemia" is a relative increase in the percentage of polymorphonuclear neutrophils, and the platelets are frequently increased in number, although both these differential findings may not be present. The absence of free hydrochloric acid in the gastric contents appears to be associated with many anemias.

Another type of anemia which may be present in patients with malignant conditions is that frequently seen in lymphoblastoma.

Case IV.—This patient is a man thirty years of age. He has noted weakness, pallor, and dyspnea beginning about five or six months ago. He has been examined many times for disease of various organs, including his heart, lungs, sinuses, teeth, and gastro-intestinal tract, but no gross lesions have been demonstrated. There is now a mass about 1 by 2 cm. palpable below the right cricoid cartilage; it is red and not adherent to the underlying tissues. There is a smaller elevated area on the skin in the lower part of the neck, about $1\frac{1}{2}$ cm. in diameter. A similar one was removed for microscopic study. The spleen is palpable 6 cm. and the liver edge can be felt 12 cm. below the costal margin. There is no ascites. The inguinal glands are not enlarged. There is edema of both feet and legs. The blood Wassermann is negative. The non-protein nitrogen of the blood is normal. The fragility of the red blood-cells to hypotonic salt solutions is normal. The spinal fluid is normal. Gastric analysis shows achlorhydria. The stool shows no blood, parasites, or ova.

One of the reddened masses in the neck was removed and on section showed the changes characteristic of lymphosarcoma. The growth was rich in lymphocytes.

The urine shows a very slight trace of albumin and a few hyaline casts, but otherwise was negative.

The basal metabolic rate was normal (+ 4 per cent.).

No tubercle bacilli were found in the sputum.

The blood count and hemoglobin percentage last week were as follows:

White blood-cells, 26,700 per cu. mm.

Red blood-cells, 2,328,000 per cu. mm.

Hemoglobin, 60 per cent. (Sahli).

Differential count:

	Per cent.
Polymorphonuclear neutrophils	65
Polymorphonuclear eosinophils	4
Polymorphonuclear basophils	2
Small lymphocytes	5
Large lymphocytes	2
Monocytes	4
Neutrophilic myelocytes	1
Eosinophilic myelocytes	1
Abnormal monocytes	16

A few of the red blood-cells showed achromia; 34 per cent. of them were reticulocytes, namely, young or immature cells that showed reticulum stained with brilliant cresyl blue. Numerous nucleated red blood-cells were seen. The variation in size of the cells was marked; 84 per cent. measured from 6 to 8 micra in diameter, and 14 per cent. were larger than this. The smallest cells measured 5 micra and the largest 11 micra in diameter. There was little variation in shape. The platelets were slightly increased, but on numerous occasions they were definitely reduced in number. Two definite types were present. One large, with a few scattered purple-staining granules in their matrix; the other, smaller, with more granules clumped around the center. Some of the platelets were as large as small red blood-corpuscles. Many had long slender processes. The abnormal monocytes were large cells with rounded light blue-staining nuclei, with a large amount of pale hemogeneous cytoplasm.

The pigment in the blood-serum was not increased. At the present time the red blood-cell count has decreased to 1,800,000 per cu. mm., and the hemoglobin to 40 per cent. (Sahli).

This case, then, is one of lymphosarcoma with progressive anemia without evidence of bleeding and without the possibility of anemia resulting from Roentgen rays. Anemia of this type is probably dependent upon invasion of the bone-marrow by the tumor. The high color index (1.3) and the variation in size of the red blood-cells are somewhat like pernicious anemia. The percentage of young red blood-cells (34 per cent.) is somewhat high for a case of pernicious anemia, but under special conditions, as during a period when very active regeneration has started, such an increase may be possible. Under such circumstances one would also expect a high white blood-cell count, as well as some of the more immature myeloid cells. The normal colored blood-serum, the normal tongue, and the absence of neurologic symptoms are features which would help to differentiate the conditions.

Case V.—This patient is a man twenty-four years of age. About sixteen months ago he noted diffuse pains developing in different parts of his body and coming on at night. Examination after the disease had progressed for four months showed discrete lymph-nodes about 1 cm. in diameter in his neck and larger ones in the axilla, and in the mediastinum. He had the peculiar Murchison or Pel-Ebstein variation in temperature with daily changes from 98° to 103° F. His white blood-cell count was 33,600 per cu. mm.

Red blood-cells, 3,920,000 per cu. mm.

Hemoglobin, 50 per cent. (Sahli).

Differential count:

	Per cent.
Polymorphonuclear neutrophils	80
Polymorphonuclear eosinophils	2
Polymorphonuclear basophils	1
Lymphocytes	7
Monocytes	10

A roentgenogram of his chest showed the numerous enlarged mediastinal glands. Examination, under the microscope, of a gland removed from the neck, revealed atypical lymphoid tissue

with numerous giant-cells and some fibrosis. The characteristics were those of the sclerosing type of lymphoblastoma (Hodgkins' disease).

The blood Wassermann was negative.

The urine showed a trace of albumin, but was otherwise normal.

The patient was given six Roentgen-ray treatments, followed by a decrease in fever and improvement in his general condition. His white blood-cell count fell to 5000, the red blood-cell count increased to 4,200,000 per cu. mm. The hemoglobin rose to 70 per cent. (Sahli). As the disease progressed the glands enlarged in other parts of his body, and these were treated with radon when they gave rise to pressure symptoms. The red blood-cell count gradually decreased so that during the course of ten months it fell to 1,056,000 per cu. mm., and the hemoglobin to 30 per cent. (Sahli). The blood-platelets were then greatly decreased and the few observed were very large. The differential count showed:

	Per cent.
Polymorphonuclear neutrophils	90
Polymorphonuclear eosinophils	1
Small lymphocytes	4
Monocytes	5

There was marked variation in the size of the red blood-cells with great differences in intensity of the staining. There was but little variation in shape. There were many shadow forms and occasionally heavily stained microcytes. Macrocytes were numerous. The patient was given numerous transfusions of blood with but temporary improvement. During the next month, the blood-cell counts gradually decreased so that the hemoglobin is now 14 per cent. (Sahli), the red blood-cells 76,000 per cu. mm., and the white blood-cells 2300 per cu. mm.

This case of Hodgkin's type of lymphoblastoma has progressive anemia, apparently without hemorrhage. Patients with this type of lymphoblastoma characteristically develop severe anemia as their disease progresses, whether Roentgen-ray or radon treatment is given or not, although, no doubt, the ir-

radiation did play some part in this case. The anemia is apparently associated with invasion of the bone-marrow with lymphoblastoma tissue.

These cases illustrate some of the features of various forms of anemia in cancer and in lymphoblastoma. Such cases make up but a small proportion of the total number of patients with malignant disease. They emphasize the point that in the absence of actual bleeding, anemia, when present, is suggestive of involvement of the bone-marrow. Contributory factors are an excess of Roentgen-ray or radon treatments and nutritional disturbances, from inability to swallow, retain, or digest the food. Temporary improvement in the condition of the blood, associated with improvement in the subjective symptoms, is a feature which may be present during the course of cancer and allied disorders.

CLINIC OF DRS. HOWARD B. SPRAGUE AND
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MASSACHUSETTS GENERAL HOSPITAL

HIGH-GRADE HEART-BLOCK UNDER THE AGE OF THIRTY

WITHOUT doubt a diagnosis of heart-block is generally considered of ominous significance; the term implies a grave disorder of cardiac mechanics. To a very considerable extent this view is justified.

But there is a group of patients in whom auriculoventricular block, either complete or high-grade partial in type, seems to be not incompatible with a reasonably symptomless life or even complete health. This group consists of the children and young people whose cardiac defect is presumably not caused, as in the older age periods, by the effects of arteriosclerosis.

In these young patients the heart-block usually seems related to one of four factors—acute general infection, rheumatism of the heart, congenital defects, or trauma. A considerable number of cases are lacking in known etiology.

Arhythmias such as auricular flutter and fibrillation, ventricular tachycardia, and auriculoventricular nodal rhythm are in many instances associated with gross pathology of the heart, yet in a few cases we find these irregularities existing as "functional" disorders, at least as far as our diagnostic tests can determine. In some instances this may be true of partial or complete heart-block.

(*a*) Of the *acute infections* which cause heart-block, diphtheria, of course, stands foremost. But when dissociation of auricles and ventricles arises in the course of acute diphtheria the patient is critically ill and in the great majority of cases does

not live long. It still remains to be demonstrated conclusively that diphtheria is the agent responsible for heart-block lasting more than a few days. A study we have recently made of 100 patients following severe diphtheria has revealed no persistent heart lesions.

Other acute diseases can result in transient heart-block. Taub[1] recently reported its occurrence in a "grip" infection in a previously normal boy, and its complete disappearance in four weeks. A patient in our series developed high-grade partial heart-block following an operation for sepsis of the jaw. Many other instances are on record of its occurrence during influenza, pneumonia, scarlet-fever, typhoid, and other infections. It is certainly not as common as a result of syphilis as was formerly supposed.

(*b*) The *rheumatic* virus seems capable of causing defects of conduction during the acute progress of the disease in the heart, possibly by pressure of local perivascular infiltration (Aschoff bodies) or edema. White[2] has reported heart-block as the first sign of acute rheumatism in 1 case—this patient is now well. Cohn and Swift[3] found some electrocardiographic abnormality in 35 out of 37 cases of rheumatic fever. There was lengthening of auriculoventricular conduction to the extent of causing dropped beats in 8 cases. Rheumatism is without doubt the cause of some instances of persistent heart-block in youth, although it is a transient condition in most cases.

(*c*) The abnormalities of heart structure found in various types of *congenital* heart disease can readily be seen to be capable of mechanical interference with the conduction system, especially in cases with septal defects. Carter and Howland[4] in 1920 collected 7 proved cases from the literature and added 1 more. White, Eustis, and Kerr[5] in 1921 reported 3 more (2 from the literature), and Romberg and White[6] in 1924 described another and added 2 from the literature. The ages at which the condition was proved have ranged from four days to twenty-three years. In most instances the block was complete.

(*d*) A very interesting group is that composed of young persons who have developed auriculoventricular dissociation

following *trauma* to the precordium. Rosenson[7] described such a case recently. A boy of ten years, with an unimportant past history, complained of weakness and a fluttering of his heart following a hard blow over the precordium. Electrocardiogram showed varying 2 : 1 and 1 : 1 heart-block and right axis deviation. The heart was not enlarged and there was only a systolic murmur at the pulmonic area. He completely recovered and was well three years later. We have seen 2 cases in which trauma was questioned as a cause of complete heart-block.

(*e*) *Idiopathic* heart-block seems to exist in a few patients. The history of infections may, however, be inadequately recorded in this group and structural damage to the conduction system might in some cases be demonstrable at necropsy. This condition has been incompletely studied as pathologic material is rarely procurable because of the good prognosis of the patient.

We are reporting in this clinic 11 cases illustrative of the 5 different etiologic groups of heart-block in young people which have come under our observation.

A. ACUTE INFECTION

Three cases seemed to be related to acute infection.

Case I.—A. B., girl, age sixteen (1926). At the age of three years she had swelling and pain in a cervical gland and it was operated upon. Following this she contracted a severe cold and a slow pulse was noted. She was carefully examined before this time and her heart was always normal. She had had infantile paralysis at three months, and her tonsils were removed at the time of the operation on her gland. There was no history of rheumatic infections. One brother died at the age of two years of pneumonia and "heart trouble."

An electrocardiogram March 9, 1916 showed complete heart-block with a ventricular rate of 50 to 55 and an auricular of 100. At times it appeared to be 2 : 1 block (Fig. 150). March 3, 1922, however, the only conduction defect was a prolonged P-R interval, 0.25 second.

When last seen, December 30, 1926, she reported that she was attending school regularly and felt well except for rather easy fatigue. She was able to skate, swim, and play ball. She had never had syncopal attacks.

Her heart showed no enlargement or murmurs. The apex rate was 78. The blood-pressure was 118 systolic and 80 dias-

Fig. 150.*—A. B. 1474. Leads I, II, and III. Partial heart-block, 2 : 1. Auricular rate 100, ventricular 50. In other records at this time the block was complete.

tolic. Electrocardiogram still showed prolonged conduction time, the P-R interval being 0.3 second.

Case II.—E. D. G., man, age twenty-four. First seen January 5, 1924. He was admitted to the Massachusetts General Hospital with a cellulitis of the neck and osteomyelitis of the jaw following the extraction of abscessed teeth. He developed precordial pain and friction rub, and it was thought he had acute pericarditis and mediastinitis. During the acute period of his illness his pulse suddenly dropped from 88 to 40, and electrocardiograms showed high-grade partial block (3, 4, and 5 to 1 ratio of auricular and ventricular beats) (Fig. 151). At times sounds suggestive of auricular contractions were heard. The heart-block disappeared in about five days and he recovered. His heart showed no signs of endocarditis and there was no

* In these illustrations the distance between abscissæ is one-tenth of a millevolt, and between ordinates is 0.2 second.

pericardial effusion. His past history was negative for rheumatic infections and diphtheria.

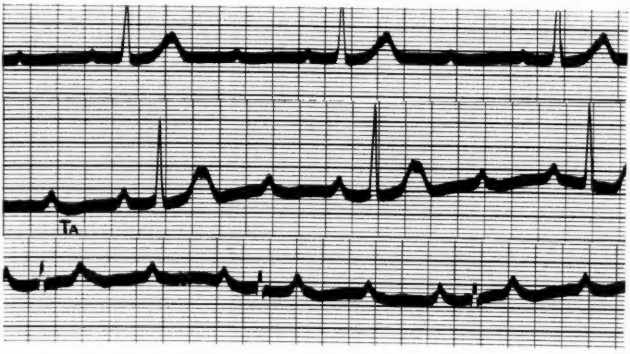

Fig. 151.—E. D. G. 8497. Leads I, II, and III. Partial heart-block, 3 : 1. A rate 105, V rate 35. Note well-marked auricular T waves (Ta).

A diagnosis of toxic or bacterial myocarditis with heart-block was made.

Case III.—P. S., girl. First seen by Dr. Edwin H. Place in 1907, age two to three years, with tonsillar diphtheria. There was a rather indefinite story of congenital heart disease which

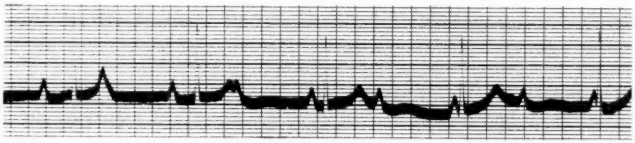

Fig. 152.—P. S. 1651. Lead II. Complete heart-block. A rate 80, V rate 43. Alternate P waves are premature. Some ventricular arrhythmia.

was not demonstrable when she was first observed. On the third day of her diphtheria her pulse suddenly dropped from 120 to 50. She recovered from her infection, but the slow rate has persisted ever since, never going above 50.

Electrocardiographic study in 1916 and 1919 showed complete auriculoventricular block, auricular rate 80–100, ventricular rate 40–50 (Fig. 152). When she was last seen in the spring of 1926

she was feeling perfectly well. There is doubt as to the actual causation of this permanent block by the diphtheria in the absence of other evidence of serious myocardial damage or peripheral paralysis, but this seems tc be a case of persistent diphtheritic heart-block.

B. RHEUMATIC

Case I.—J. I. P., boy, age three years. This child was brought to the Children's Clinic of the Massachusetts General Hospital April 18, 1924. He was a normal baby at birth but had had bronchopneumonia at three months, frequent colds and sore throats, and mumps at two years. There was no known rheumatism. Four weeks before he had caught cold and had fever. His local doctor had diagnosed bronchopneumonia. The slow pulse was noticed by his mother at that time.

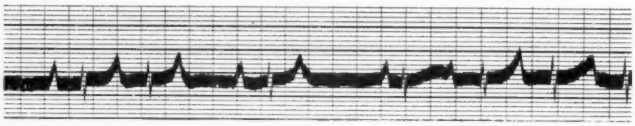

Fig. 153.—J. I. P. 10,777. Lead II. Partial heart-block 2 : 1 and 1 : 1. A rate 110, V rate 80. Sinus arrhythmia. P-R interval 0.16 to 0.28 second. High sharp P wave.

He was seen in the children's cardiac clinic. Examination showed a pale, rachitic, child with large inflamed tonsils and a loose cough. The apex impulse of the heart was 5 cm. to the left and there was a blowing systolic murmur over the precordium and a rather harsh diastolic murmur loudest along the left sternal border. The second sound was reduplicated at the apex and there were numerous dropped beats. A diagnosis of rheumatic heart disease with aortic regurgitation, partial heart-block and dropped beats was made. Electrocardiogram revealed a lengthened P-R interval, 0.35 second, and occasional dropped beats with a rate of 95, and left axis deviation. He was admitted to the hospital.

Further study showed periods of 2 : 1 block with an auricular rate of 120, and a ventricular of 60. There was a high, sharp P wave in lead 2 (Fig. 153).

He improved while in the hospital and was discharged in fair condition after tonsillectomy. When seen six months later partial heart-block was still present up to 3 : 1. A month later a history of rheumatism in the feet following his pneumonia was secured. His sister was convalescent from chorea. He had had two fainting attacks. It was felt that aortic and mitral lesions of rheumatic origin were present and that rheumatism rather than a congenital defect must have been responsible for the heart-block as his heart was reported normal at the Children's Hospital during pneumonia at the age of three months. A pneumococcus infection of the heart seemed very unlikely.

He was last seen July 14, 1926. His heart condition was unchanged, although he had had a severe respiratory infection during the winter.

Case II.—K. C., girl, age eighteen years. First seen October 22, 1924. The patient had been in good health until three months before she was seen, when she began to have acute pains in the right lower quadrant of the abdomen, which was diagnosed appendicitis. This subsided gradually under treatment of rest in bed and ice-bags. At this time her heart rate was found to be 42, and since that time it had been 32 to 48, generally near the lower limit. At the time of the acute attack she fainted and had also fainted once since that time. These were possibly attacks of Adams-Stokes syndrome. When examined she said she felt perfectly well except for easy fatigue and shortness of breath on moderate exertion.

There was no history of rheumatism in the family.

Past History.—She had always been very well except measles at the age of eight years, and chronic catarrh and tonsillar infection for several years. On physical examination in the past she had always been considered healthy. Two months before the onset of her illness her heart was said to have been normal.

Physical Examination.—Well-developed and nourished, normal breathing, and color. Her tonsils were very large and inflamed with enlargement of the cervical glands. The cervical veins were not engorged, but there was venous pulsation with

easily seen auricular waves falling between ventricular ones. The heart showed definite enlargement, the apex impulse being felt in the fifth space 9 cm. to the left of the midsternal line and 2 cm. beyond the midclavicular line. There was no increase in supracardiac dulness. The heart-sounds were slow, the first sound at the apex decreased and almost masked by a very harsh, loud systolic murmur which was heard all over the precordium, but loudest at the apex. There were no diastolic murmurs. At the lower end of the sternum there were faint auricular sounds in ventricular diastole. The ventricular rate was regular at

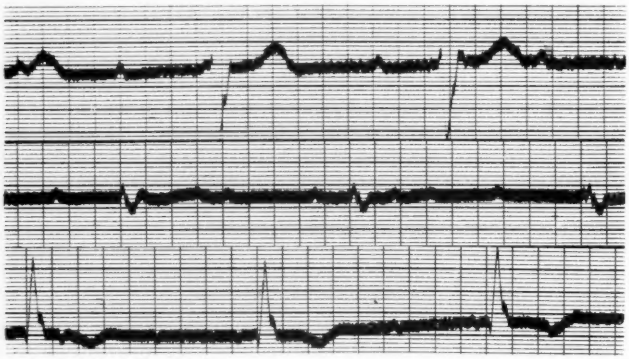

Fig. 154.—K. C. 8436. Leads I, II, and III. Complete heart-block. A rate 100, V rate 33. Intraventricular block of the left bundle branch type.

34. There was no evidence of congestive failure in lungs, abdomen, or legs. The blood-pressure was 119 systolic and 55 diastolic.

Electrocardiogram showed complete auriculoventricular block with an auricular rate of 85 and a ventricular rate of 35. There were rather small complexes in all leads, a deep T wave in lead I and a high T wave in lead III.

Tonsillectomy was advised and performed about two weeks later.

December 2, 1924, she reported feeling well. The findings were the same except that electrocardiogram showed in addition

left bundle branch block. This was also present March 20, 1925, the auricular rate being 105 and the ventricular 33 (Fig. 154).

It seemed clear that she was suffering from a progressive carditis. A report from her doctor in January, 1927, stated that she had felt about as usual until September 7, 1926, when he was called to see her because of severe distress on waking in the morning. When he arrived her pulse rate was 24 and she died in a few minutes.

C. CONGENITAL

Case I.—E. A., girl, age twelve years. She was first seen in the clinic May 7, 1924, having been sent in for an opinion by a school physician. She had no symptoms and had led an active life. Aside from measles, chickenpox, and several attacks of

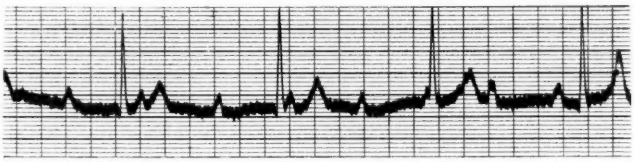

Fig. 155.—E. A. 9442. Lead II. Complete heart-block. A rate 100, V rate 50.

tonsillitis there were no infections in her past history. Her slow heart was first noticed at the age of four years by the doctor present at birth who did not discover anything wrong at that time. Her tonsils and adenoids were removed at the age of six years.

Physical examination was negative except for the heart which was slightly enlarged to the left and showed a loud blowing systolic murmur over the precordium, maximal at the fourth left rib near the sternum. The rate was 40 to 60.

At that time a diagnosis of probable congenital heart disease with interventricular septal defect and partial auriculoventricular block was made. The electrocardiogram showed partial block, 2 : 1, ventricular rate 45, auricular 90. An electrocardiogram December 3, 1924 showed complete heart-block, auricular

rate 110, and ventricular rate 44 (Fig. 155). September 16, 1926, she reported to the clinic. She felt perfectly well, but there was no change in the cardiac findings. Complete block was still present, auricular rate 110, ventricular 50.

D. TRAUMA

Case I.—M. W., female, age forty (1927). This patient was a nurse; seen January 12, 1927. She said that there was "heart trouble" in her mother's family, and one brother had died of heart disease. She had diphtheria at one and a half years, but had not had rheumatic fever, chorea, tonsillitis, or scarlet fever.

At the age of fourteen she fell on a stairway and hung by one hand to a door frame holding a pail of water in the other hand.

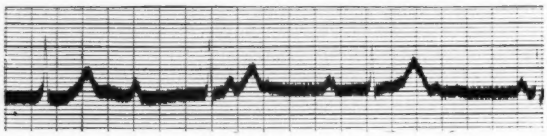

Fig. 156.—M. W. 12,367. Lead II. Complete heart-block. A rate 75. V rate 45.

Immediately following this she felt very badly, although there were no external injuries. Thereafter, whenever she became fatigued, she had peculiar spells of complete exhaustion. At the age of eighteen she began counting her pulse during these spells and noticed it was very slow, 38 to 40. Between attacks it was 50 to 60. In 1925 complete heart-block was discovered at another clinic. She had no symptoms except easy fatigue and some dyspnea on exertion. Following appendectomy (1917) and gall-bladder operation (1923) she had had attacks of nocturnal palpitation in which her heart beat violently and apparently rapidly. She had no syncopal attacks. Superficial examination showed no important murmurs in her heart.

Electrocardiogram January 12, 1927 showed complete heart-block, auricular rate 75, ventricular 45 (Fig. 156).

E. UNKNOWN ETIOLOGY

Four cases are here reported in which no satisfactory explanation of the heart-block could be found.

Case I.—C. E. A., girl, age twenty-four years. Seen February 4, 1917, and was admitted to the Massachusetts General Hospital. She said that her general health had never been good and she was easily fatigued. She had had diphtheria and scarlet fever at eighteen months of age, and a severe sore throat four years before admission. Her mother said that at the age of twelve years the girl had had an irregular heart. Eight years before entry increasing fatigue became prominent with aching of the arms and swelling of the left hand. She was thought by her doctor to have myxedema and had been given thyroid substance without relief, but had been made toxic by it. She was

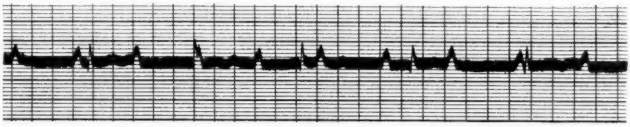

Fig. 157.—C. E. A. 2127. Lead I. Complete heart-block. A rate 96, V rate 60.

studied by the cardiac department in order to find out the cause of her bradycardia in the presence of thyroid toxicity.

Examination was essentially negative except for her heart, which was enlarged as shown by *x*-ray, the increase being largely to the right in the region of the auricle. There was a systolic murmur loudest at the third left space. The pulmonic second sound was accentuated. Electrocardiogram showed complete auriculoventricular dissociation with variable auricular and ventricular rates, 72 to 120, and 50 to 64, respectively. The auricular tachycardia was explained by the hyperthyroidism and the ventricular bradycardia by the finding of heart-block.

In October, 1920, the same complaints resulted in readmission to the hospital. The findings were as before, but the auricular rate was 96 and the ventricular 60. Her blood-pressure was 116 systolic and 70 diastolic (Fig. 157).

Since then she has been able to work as a teacher most of the time, although dyspnea, palpitation, and weakness are troublesome at intervals. She was last seen June 2, 1926, and reported some improvement from the use of bromids and strychnin. Her pulse rate recently has remained constantly under 50. Her last electrocardiogram was March 26, 1925, the auricular rate was 80, the ventricular 50.

Case II.—K. M. F., girl, age twenty-six (1918). This patient was referred in 1917 for electrocardiogram at which time complete heart-block and low voltage of the Q-R-S complexes were demonstrated (Fig. 158).

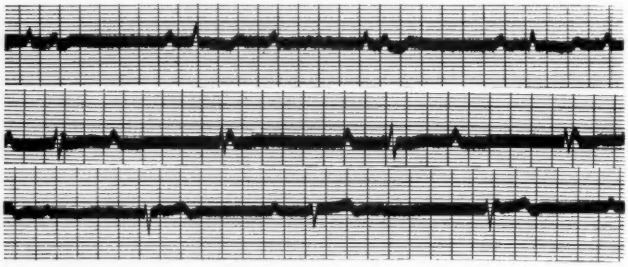

Fig. 158.—K. M. F. 2243. Leads I, II, and III. Complete heart-block. A rate 50, V rate 36. Low voltage of ventricular complexes in all leads.

Past History.—She had diphtheria at the age of three, and malaria from seven to fourteen years of age. She was a sprinter in High School. At the age of twenty-five (in 1917) she had an accident, falling on the ice and becoming unconscious followed by soreness where her corset had "dug into her chest." After this her heart was first noticed to be regular and slow, although her doctor said that for two years before this it had been irregular and slow, suggesting partial heart-block.

Her physical examination (November 25, 1925) was essentially negative except for her heart which showed the apex impulse in the fifth space 10 cm. to the left of the midsternal line

and 2 cm. beyond the midclavicular line. There was a loud, blowing systolic murmur, without thrill, over the precordium, maximal half way between the apex and the pulmonic area. The rate was regular at 40, and the auricular sounds were heard distantly. The blood-pressure was 140 systolic and 80 diastolic.

She was entirely symptom free and able to play 18 holes of golf a day without trouble.

The electrocardiogram on November 2, 1926 was unchanged: complete heart-block, auricular rate 60, ventricular rate 40, and low voltage of the ventricular complexes.

Case III.—P. S., girl, age twelve. Entered the Out-patient Department December 12, 1923 because of forceful heart beat.

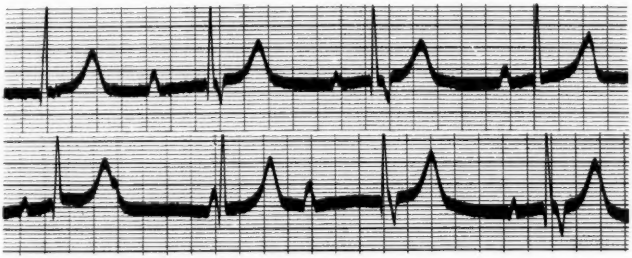

Fig. 159.—P. S. 8320. Lead II. Complete heart-block. A rate 75, V rate 42. Note the variation in P waves. The second and third ventricular complexes in the first strip and the third and fourth in the second strip are followed by inverted P waves, possibly due to retrograde conduction, but more probably only premature auricular beats.

She had had no tonsillitis, rheumatism, chorea, scarlet fever, or diphtheria. She was not a blue baby at birth.

Her tonsils appeared normal, but the tonsillar glands were palpable. Her heart was enlarged, percussion dulness being 9 cm. to the left. The heart sounds were sharp, and there was a fairly loud blowing systolic murmur heard best at the lower left sternal border with a short mid-diastolic at the apex. No thrill was felt. Electrocardiogram showed complete heart-block,

auricular rate 85, and ventricular 45. The apex rate between December, 1923, and April, 1924, varied from 64 to 44. The blood-pressure was normal (Fig. 159).

She was last heard from December, 1926, at which time she felt well and was walking 3 miles to school every day. She did not keep her promise to report to the clinic.

This patient may have a rheumatic infection of the heart. Without further data we cannot be sure.

Case IV.—L. S., male, age twenty-eight (1926). This patient had been followed in the Out-patient Department since 1904. In 1909 he was said to have shown cardiac enlargement, a systolic murmur at the apex, and a rate of 60. There was an indefinite story of rheumatism at the age of five years, but no

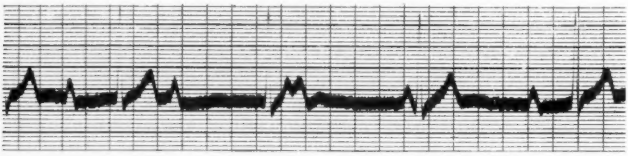

Fig. 160.—L. S. 10,674. Lead II. Complete heart-block. A rate 70, V rate 50. Some auricular arhythmia.

diphtheria. At the age of seven years he had had an attack of partial syncope. He was very neurotic with many gastro-intestinal complaints. In 1915 he had lobar pneumonia followed by toxic psychosis.

On January 7, 1926 he was seen in the cardiac clinic because of precordial pain. The apex of the heart was in the fifth space, 8 cm. to the left, just inside the midclavicular line. There was a precordial systolic murmur heard at the apex, left sternal border, and pulmonic area. The rate was 48. His blood-pressure was 120 systolic and 80 diastolic.

An electrocardiogram showed complete heart-block, the auricular rate being 64 and the ventricular 50. This had been discovered eleven months before at another clinic. He was last seen January 13, 1927, and his condition was unchanged.

In this case no definite cause can be assigned to explain the block which may be congenital or rheumatic in origin. Coronary disease seemed very unlikely. It was felt that the pain was more typical of duodenal ulcer than of cardiac disease and it was not relieved by nitroglycerin, but gastro-intestinal *x*-rays were negative.

SUMMARY

We are reporting in this clinic 11 cases of high-grade heart-block occurring under the age of thirty. One of us has previously described three others of probable congenital origin and one other seen at the onset of rheumatic fever. During the past twelve years, there have been in addition 2 patients under thirty observed in our clinic who have had delayed auriculo-ventricular conduction, to the extent of causing dropped beats, not due to digitalis.

The heart-block in the cases here described was complete in all but two, and of high grade in the latter. It is interesting, however, to note that the ventricular rates in the idioventricular rhythm were almost always high: in only 1 case was it under 40, in 7 cases it was between 40 and 50, and in 1 case 50 to 55. One patient whose ventricular rate was usually about 50 reached 80 when she was toxic from thyroid extract.

The cases considered in this clinic illustrate the main etiologic groups of heart-block in young people. They show, moreover, that while this arhythmia may develop coincidently with general infections or rheumatic processes, or may be evident at birth, many times it may arise unheralded by any grave disease. It seems fair to assume, and it is supported by our experience with such cases, that the lesion or mechanism responsible for this defective conduction between auricle and ventricle, is not a serious progressive process. The prognosis as regards life, in the absence of marked and demonstrable cardiac disease, we believe to be essentially good. The future, as far as the conduction defect is concerned, depends frequently upon an unknown factor and cannot be foreseen.

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CLINIC OF DR. BRONSON CROTHERS AND
MARGARET WIRT, A. B., M. S. S.

CHILDREN'S HOSPITAL

THE MANAGEMENT OF MENTAL DIFFICULTIES IN A PEDIATRIC CLINIC

IN any general hospital for children the doctors have a more or less isolated if lively time. Therefore, it is obvious that pediatricians, like other specialists, should emerge from time to time in order to view the general medical world and acquire new ideas. On one such mental shopping trip a few years ago it became apparent that styles in children's ailments had changed. Furthermore, almost everybody but the pediatricians knew that they had changed. The very young generation no longer suffered from teething or indigestion or mumps, but they languished under the weight of complexes and mal adjustments. The non-matured ego of the parent was evidently a greater threat than the tubercle bacillus and not as easily recognized.

We tried to laugh at the new style but found to our distress that it was no laughing matter. On looking frankly at the situation it was perfectly clear that the mental and emotional life of children had been neglected by most of us. When this point became clear we decided to investigate the problem more carefully. We at once found an accessible body of literature and, better still, expert advisers. The National Committee for Mental Hygiene has published a magazine for some ten years, and there are many volumes on the subject available.

Having discovered the literature we were a bit appalled at its size and complexity. But pediatricians share with general practitioners a certain facility and arrogance in borrowing

information and technic and using it. We do not hesitate to pick up attractive bits of chemical theory or alluring endocrine hypotheses and use or abuse them. So the mere fact that human behavior is a rather formidable subject didn't repel us.

The library period of investigation lasted in an acute stage for many months. We read all the articles on children in "Mental Hygiene." We read most of the easily accessible books on child psychology, we made forays into more technical fields and read Freud, Stekel, Jung, Adler and various interpreters and disciples and perverters of each. We dipped into psychology and read Watson on behaviorism, Terman on mental tests, and Healy on delinquency. Then we left the library and came up for air.

It was perfectly clear that all of the experts couldn't possibly be right at all points and yet it was hardly conceivable that they could any of them be all wrong. We came to the conclusion that all these people had one quality in common, they were tremendously interested and spent a great deal of time thinking about children. As a practical matter the question we had for decision was whether to attempt to deal with the problem ourselves or to send all our problems to more experienced people.

The next step was to see what was happening elsewhere. We watched mental testing, we looked in at endocrine clinics, we visited psychopathic hospitals and court clinics and got a very general impression of methods. We checked our impression by attending meetings addressed by propagandists. Out of this admittedly superficial survey we gained enough of an idea of the problem to justify us in making plans.

On the whole it seemed rather absurd to attempt to transfer the whole weight to the eager shoulders of the psychiatrists. We had learned in our literary travels that the "amour-propre" of the child should not be wounded, and we rather objected to the idea that only the psychiatrist cared for the whole personality. We might be relegated to the ignominous position of practitioners of "part medicine," but not without a struggle for the integrity of our own "amour-propre" and our own standing as general practitioners among children.

In a hospital planned for the care of physical disease there are, of course, many children with defective intelligence, bad habits or chaotic emotional states. If all of these were to be transferred we would lose sight of most of them. We weren't as good psychiatrists as others, but we clung to the idea that others weren't as good pediatricians as we. Then again routine reference had been tried. We found that only a few ever reached the special psychiatric clinics to which we sent them. Obviously the stragglers had to be marked down as therapeutic failures. In addition many of the more formal clinics could take only occasional cases.

We then tried the experiment of having a highly trained psychiatrist come in from time to time. This method didn't work out at all. In the first place the modern psychiatrist seems to us to be just a bit too acquisitive to be trusted among a lot of children who are not in the best of physical health. The new recruits started off with ideas which were certainly elaborate. One placed a list of habits and customs which he regarded as of psychiatric interest upon a bulletin board. He planned to classify all these children and follow them long enough to find out how they came out. Three major objections came up. First, we have an age limit of twelve years. This hardly gave time for dementia præcox and the other psychoses to show their faces. Second, the list of possible psychiatric conditions included almost everything except infections and surgical conditions and required rather more generosity than could be expected of the medical staff. Third, the proper management of research of the type proposed requires many trained assistants. Another transient visitor worked with us for awhile, afterexperience in doing really careful psychiatry in an admirable clinic. He would look at a child who was misbehaving and announce quite properly that the child needed a "personality study." He was shown a room and invited to enter with the child and go to it. This seemed to him quite absurd. The child had not been psychometrically tested, it would take many visits, he couldn't quite see how in the confused atmosphere of the clinic it could be done.

Now it may well be that good psychiatric work with children cannot be done except with elaborate personnel and unlimited time. On the other hand, it seems clear to us, if that is true, that most children will not get it at all, now or in the future. It is quite obvious that the clinic which takes two or three new cases a day will be able to handle only a fraction of the problems which are said to exist.

After these half-hearted attempts to solve the difficulty by reference to other clinics or by importation of people who would play with us on our own terms, we decided to start fresh and see what we could do ourselves. With this idea in mind we reviewed our experiences with a good deal of humility. However easy it may be to pick flaws in a method, it is no joke to try to build up a going machine from a series of borrowed parts, and that was what we set out to do.

Like a child at New Year's we made a series of resolutions. These were goody-goody and rather banal. They were as follows:

1. We will borrow only tools we intend to use. Of these, patience, industry, and interest are obviously the most valuable at the start.

2. We will try to place very difficult cases in the hands of those better qualified to care for them wisely. In particular we will so refer such cases as may end in legal delinquency.

3. We will use only words which we understand and we will enlarge our vocabulary with the greatest reticence and only as new ideas dawn upon us.

The first resolution involved more than was apparent at the start. It was clear that we must settle down with children with mental difficulties and see if we could find out about them. The most cursory consideration showed that a social worker especially interested in this type of problem was absolutely essential. As long as we needed a social worker we decided to plunge and get one who could bring special assets as well. By good luck we obtained one who had been trained in psychiatric social work, had had experience in a clinic for the correction of habits and had had a year's work on the medical service. Obviously we had

thus borrowed from the psychiatrists a great section of their assets in a singularly successful way. The raid, however, had been rather costly and we couldn't add to our loot by acquiring a psychologist. However, we were well started and prepared to make good on our first resolution.

The second resolution was not hard to fulfil. In spite of knowing that we intended to try to practice unorthodox mental medicine we found the psychiatrists and psychologists ready to co-operate at every turn. Where before we had simply given an address to a patient's mother, with no assurance that she would follow it up, we now knew what to expect and knew whether they went where they were told to go. Furthermore, we could interpret the technical reports we received.

The third resolution was the hardest to keep. We caught ourselves occasionally, and others caught us more often, using technical terms which we did not understand. These difficulties are diminishing as time goes on. In the first place, we like to think that some of our ideas have grown enough to warrant adoption of certain technical terms, and in the second we no longer try to use most of the language of modern psychiatry.

In moments of expansiveness we have felt rather cocky; in moments of depression quite futile. This alternation of mood no longer distresses us. We know by now that certain problems are quite insoluble. For example, if parents absolutely refuse to co-operate or to submit themselves to reasonable study, we mark the case off as a total loss. At first we did this rather casually. As we have gone on we do it reluctantly and after repeated explanations. The child who is feeble-minded and is not curable by medical measures we recommend to an institution, or try to fit into a modified educational régime. Then we drop the problem for the time being.

The children we are most interested in are the ones with anxious, often misguided parents or unwise teachers. Here we get to know the parents, the teacher and the child as far as we can. By repeated efforts, we have found various plans which can be proposed.

Balancing up the advantages and disadvantages of our

method, and comparing it with more formal arrangements, we believe that we start off with less load than the psychiatrist. The loyalty of the mother has already been given to the pediatrician, since the idea that doctors have some authority over habits, as well as over prescriptions, is already established, since the supervision of infant feeding became a medical task.

Moreover, under a system by which one doctor cares for the body and one for the mind, conflicts of authority and waste of time and energy are inevitable. Also patients can be very easily and simply transferred after a preliminary study when they will not go at first.

On the other hand, we admit that our scheme would be distinctly incomplete without the loyal co-operation of more specialized clinics. We have probably borrowed more than we realize from psychiatry and perhaps we should be judged as psychiatrists and not as pediatricians. This possibility appalls us a bit, for we feel quite helpless in many of the fields where psychiatrists walk undisturbed. In any case, we have read and practised and read again, consulted with psychiatrists and disagreed with them, and have worked out a method which under favorable circumstances seems to be feasible. We have not been willing to admit that most of the problems which turn up in a medical clinic cannot be treated there, provided a few doctors and a social worker stand ready to spend time and energy upon them.

In any case the effort has been abundantly worth while for the sake of demonstrating the validity of current psychiatric views as to the necessity of doing something about children who don't get on well. Any intelligent doctor who wishes to can go over the intellectual road we have traveled. He may or may not follow it to our conclusion. Fortunately, there are constant alternative paths. He may arrive at a psychoanalytic or a behavioristic goal, but at least he has seen more of the world than one who never travels. We have come back to work as pediatricians and intend to profit by our journey if possible.

Now all this introduction is mere padding unless we can show how it works out. We therefore propose to inflict a few

case histories. In these histories we will show where we refused to follow trails as well as the places we went on to the extent of our knowledge.

Case I.—An attractive small boy of three and a half years was brought to the hospital because he had thrown his baby sister out of a second story window. Fortunately the infant caught in a gutter of the porch roof and was not hurt. We had a very brief interview with the mother and heard about tantrums which were combined with rather skilful planning of mischief.

Physical examination showed nothing abnormal. A mental measurement revealed the expected superior intelligence. No one with our extensive literary experience in psychiatric technic could have failed to realize that the boy was a proper subject for profound technical research. We at once called up the psychiatric clinic associated with the Juvenile Court. Unfortunately they felt that he was too young. We urged the point of view that attempted infanticide was obviously delinquent behavior, but they were firm and suggested a Habit Clinic. For some reason, we couldn't quite see why throwing babies out of the window should be allowed to become a habit or be treated as such. The solution that appealed to us was a psychopathic hospital. We urged this course upon the mother, but she flatly refused to go. The highly perilous situation was thus left on our hands and repeated attempts to shift it to more competent supervision failed.

We were forced into studying the various people concerned. The father is a taxi driver, apparently a cheery honest soul, who is trying his best to make a proper home for his family. Unfortunately he is forced, by an inadequate income, to live with his parents. The mother, a thin anxious woman, is jealous of her husband, and helpful neighbors suggest that taxi drivers are suspicious characters with opportunities for unfaithfulness.

The small boy realizes fully that there is difficulty between his parents and takes every opportunity for increasing it. The incident for which he came to us is only one of a series of unfortunate episodes. If he is punished he announces a plan of reprisal

which he carries out quite competently. He may say he will bite the baby or he may tell some outrageous story of abuse to the father on his return.

By this time we were well beyond our depth in psychiatric waters, but we realized that the mother needs understanding which she can get at a psychopathic hospital. The rest of the adult members of the family see this clearly enough, but the mother suspects a plot. Meanwhile, we are keeping track of the boy and he is quieting down. We feel that some part of his improvement is due to increased tolerance all round.

As we got into the story it seemed clear to us that a good deal of the difficulty could have been avoided if the various doctors who had taken care of the mother had tried to understand her a little, instead of merely trying, unsuccessfully, to add to her weight. As the situation now stands a very unsatisfactory status is maintained, but at least we stand ready to help and know where to get further help when it is asked.

Case II.—Anna C., ten years old, was operated upon at another hospital for appendicitis in November, 1924. The vomiting which had led to the operation persisted and a second operation was done a few days later. No obstruction was found. After a rather stormy period, during which she was tube fed, the family removed her from the first hospital and tried to care for her at home. The vomiting and pain persisted and she came to the Children's Hospital on January 12, 1925 and stayed a month.

A most rigid study of her physical condition gave no clue suggesting any valid line of attack. The child was apathetic and unresponsive and seemed to everyone abnormal mentally.

We then tried to solve the question by applying special mental technic. The experienced psychologist who tried to get psychometric measurements could not accomplish much as the child vomited and refused to co-operate. It was clear that her physical condition did not warrant moving her to a psychopathic hospital for study. Consultation with psychiatrists in the ward got nowhere in particular, as the physical and mental elements were thoroughly confused.

We thought it over and rather despondently took up the problem as best we could, not because we felt effective, but because we couldn't dodge it.

The family were intelligent prosperous people with three other children. The patient was next to the oldest. Everyone else was all right.

Anna was in a special class for backward children and was not easily managed even there. At home she was untidy, vain, and sensitive. We talked with the teacher and the parents and got a very definite idea of the difficulty of the situation.

Obviously the best plan was to get the child away for a considerable time under known conditions of hygiene and discipline. We presented the plan, but not unnaturally the parents declined to have a seriously sick child away from home. Since home had been chosen we went into the question of discipline and routine most carefully. It was clear enough that vomiting after two laparotomies is a proper cause for anxiety, but we tried to get the mother to ignore it as far as possible.

The very uncertain plan worked out fairly well. The vomiting stopped after a few times. The child became talkative; on the whole she gradually became as efficient as her admittedly defective intelligence allowed.

The whole problem in this case was confused. We felt that the mental side of it was of great importance. Yet it is very clear that most meticulous ruling out of physical factors was necessary. Quite probably the initial laparotomies were unavoidable, but they had added to our difficulties. The additional information acquired by our investigation was easily obtained by entirely non-technical methods. The attempt to apply more elaborate psychiatric methods failed to help us.

We realize that we are only establishing a rather unsatisfactory status, but we are sure that we are able to understand the situation fairly clearly. The family are far from a solution, but we have kept in touch with them and in any new complication we can help them by suggestions or by arranging for permanent care. Unless someone has all the facts, recurrent attacks are likely to be followed by recurrent operations.

Case III.—As we found case after case where careful, friendly, non-technical collection of social data helped us to understand and often to improve the management of children, it became obvious that the problems were not all due to ignorance or poverty. Private cases frequently needed just the sort of supervision which had proved helpful in the clinic.

For example, a child of eleven years from another city was brought to one of us because she had stopped going to school. The seriousness of the situation was obvious. In the first place the child was physically in very poor condition. She was tall and thin and had grossly defective posture. The more interesting matter was the series of events leading up to her refusal to go to school. Apparently a nearby fire had alarmed her and she felt frightened at the idea of being caught in a burning building. Moreover, she was gradually refusing to do various ordinary things, giving all sorts of inadequate excuses or even going into tantrums when a course of action was forced upon her.

The mother had read much upon methods of bringing up children, but had arrived at no very useful conclusions. She was eager to understand and explain everything and was afraid that she would tell some untruth. Feeling quite certain that complete frankness was desirable she had carried on long conversations with the child. Afraid of imposing rules she had embarked on a series of compromises. For instance, open fires were indulged in only on rainy days.

The question here could have been attacked in either of two ways. In the first place posture could have been corrected and by rest and dietary supervision a more satisfactory physical status could have been reached; or the physical side could have been ignored and the mental problem attacked. Either way alone seemed unsatisfactory, but the seizing of both horns of the dilemma at once seemed feasible.

The urgent question which needed decision was whether adequate treatment was possible at home. Miss Wirt spent a day or two at the house and talked with various people. The father and mother, thoroughly sophisticated people, were very sensitive, rather timid individuals who were entirely frank about them-

selves. The teacher at the school was very dubious about any plan which involved return of the child to her. We could see no reasonable prospect of solving the difficulty by advice. The elaboration of an adequate alternative plan happened to be easy. An admirable open-air school near Boston and a home with a teacher who had handled many difficult problems were available.

The next step was the stating of the situation in such a way that full co-operation could be obtained. We felt that the child had been using thoroughly unacceptable ways of achieving her desires. Whether we labeled her psychoneurotic or constitutionally inferior or what not seemed quite immaterial. In any case an emergency existed, educationally, physically, and emotionally. We proposed our plan as a sensible solution. Knowing that indecision was a characteristic of the parents we arranged a meeting of all concerned so that acceptance could be followed by immediate action.

As a result, the child was taken into a school where fire risk didn't have to be considered—she liked it and did well. At the same time an enthusiastic orthopedist corrected her posture and thinks to this day that fear of fire can be eliminated by correction of faulty bodily mechanics. In any case the child after a few months went back home, goes to school, has seen fires without emotion and is, as far as we can see, doing entirely well.

In this case again the facts were collected and a plan of action taken without psychiatric formulation of any theory. It was clear that a prolonged personality study would have revealed all sorts of material. But in any case we do not see that any great harm has been done.

These cases have been discussed without using technical psychiatric words. We have neither psycho-analysed them nor have we psychometrically rated them in any adequate way. In each case we have used common methods and we hope common sense. On the other hand, the background obtained by reading and observing psychiatric work has unquestionably led us to ask questions and advise treatment which we would other-

wise have omitted. In many ways the effort to devise an effective method for management is worth while. In the first place, the importance of the problems of mental difficulties is made clear. Second, the futility of careless advice becomes evident. Third, the attempt to do it oneself leads to a realization of the complexity of some of the problems and to useful consultation with others.

We realize that the method we use is only one of many. But at least it is better than none and we feel that for us it is the best one. We have, however, no quarrel with other and more elaborate methods; indeed, they are obviously essential. We, for the moment, feel that most of the mental and emotional difficulties of childhood can be and should be cared for by pediatricians, always granting that pediatricians are industrious, patient, and eager students of the "whole child."

CLINIC OF DR. CLEMENT I. KRANTZ

THE MEDICAL SERVICE OF THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL OF HARVARD UNIVERSITY

TWO CASES OF LYMPHOBLASTOMA WITH INCREASE OF BASAL METABOLIC RATE

INCREASED metabolic activity is characteristic of certain conditions among which are the leukemias and hyperthyroidism. A comparison of these two diseases has brought out the fact that many symptoms are common to both as the result of increased heat production. Such symptoms are: an increased pulse rate, easy fatigability, usually an increased respiration, both in rate and volume, a sensation of warmth, an increased tolerance for cold, a warm, moist skin and not uncommonly sweating. Besides these symptoms an increased appetite occurs, and this may be associated with a progressive loss of weight. This loss of weight will not continue if the primary condition is alleviated or if the caloric food intake is increased so as to balance the augmented metabolism. These symptoms of hypermetabolism vary with the degree of rise or fall in the basal metabolic rate.

When an increased metabolic rate is found, there arises the question of whether or not thyroid overactivity is present. Not only must myelogenous leukemia be excluded, but also the different forms of lymphoblastoma of which lymphatic leukemia, pseudo leukemia (aleukemic lymphatic leukemia), Hodgkin's disease and lymphosarcoma may be considered types. The symptoms of increased metabolic activity may be present in some such cases, and occasionally such signs as exophthalmos and even, perhaps, increase in the size of the thyroid gland may be demonstrated. It is possible to have hyperthyroidism and some form of lymphoblastoma occur in the same patient. Thus

it can readily be seen that fundamental disease of the blood forming tissues may exist and yet the patient receive treatment for disease of the thyroid gland, whereas the primary condition itself should indicate the type of treatment pursued. The following cases illustrate this point:

Case I.—A Jewish boy, twenty-one years of age, an upholsterer by trade, first reported to this clinic thirteen months ago, complaining of swelling in the right side of his neck. One and one-half years prior to this he had a slight cold followed by stiffness of his neck, after which he noticed some small "lumps" appearing in the right cervical region. These "lumps" varied slightly in size from time to time, but he believed that similar swellings had never occurred elsewhere in the body. Fifteen months ago another group of symptoms appeared, consisting at first of some weakness and increased fatigability. These grew progressively worse up to the time of hospital entry. He noted at this time that: (1) he had become distinctly more pallid and more "nervous"; (2) his fingers tended to have a fine tremor; (3) about twice each week he had had a drenching night sweat; (4) his eyes had become gradually more prominent, varying occasionally in degree, but were a little less prominent recently than during the previous months; (5) he had not observed any increase in size of the anterior aspect of his neck, nor did he feel that there was any throbbing or pulsation present; (6) when walking or climbing steps, shortness of breath was rather marked, but he had had no peripheral edema or other symptoms suggesting cardiac disease; (7) he had lost about 20 pounds in weight. This could be accounted for by his rather poor appetite, so that he had eaten less during the past few months. At this time his bowels were regular. He gave no history of diarrhea since the onset of his present condition. The day before hospital entry he had felt a little "feverish."

The family history was negative.

In the past there had been no disorders of importance that were considered to have any bearing on his present condition except that he had suffered from repeated sore throats and colds.

He had always been rather "nervous" and high strung, but more so since his present illness.

Physical Examination.—Thirteen months ago physical examination revealed a pale, undernourished and underdeveloped boy, who was quite restless, but in no great distress. His skin was smooth and moist and of normal warmth. The eyes were a little prominent and a slight lid lag was present. Extra-ocular movements showed no abnormalities. The tongue showed a slight tremor on protrusion. The tonsils were not enlarged or red. A lymph-node measuring 4 cm. in diameter was present below the mastoid region and lateral to the sternocleidomastoid muscle. This node was firm and hard in consistency, yet freely movable and neither tender nor adherent to the overlying skin. Smaller nodes were palpable behind this muscle, varying in size from a few millimeters to 1 cm. in diameter. Similar small lymph-nodes were felt in the left supraclavicular fossa and in the inguinal regions. The axillary nodes were enlarged and several measured about 1 to 2 cm. in diameter. The thyroid gland was just palpable, but no bruits or thrills could be made out. Lung and cardiac examinations revealed no abnormalities. Percussion demonstrated abnormal dulness in the supracardiac region. A roentgenogram of the chest showed a lobulated mass in the mediastinum. This had sharp outlines and suggested enlarged mediastinal lymph-glands. On fluoroscopic examination the vault of the diaphragm on the left side was found to be higher than that of the right. In the abdomen a fairly firm, non-tender spleen was felt which extended 5 cm. below the costal margin and the liver edge was palpable on deep inspiration. The extended fingers showed a moderately fine tremor. His weight was 108 pounds.

The patient was then given one treatment with radon over the neck and in each axilla. At this time the basal metabolic rate was 38 per cent. above normal with a basal pulse rate of 108.

A cervical lymph-node was removed for diagnosis and the pathologist reported that a lymphoblastoma of the Hodgkin type was present.

Blood examination revealed the following findings:

Hemoglobin (Sahli)	60 per cent.
Red blood-cells	3,440,000 per c.mm.
White blood-cells	6,900 per c.mm.
Differential count:	Per cent.
Polymorphonuclear neutrophils	65.0
Polymorphonuclear eosinophils	3.0
Polymorphonuclear basophils	1.5
Lymphocytes, small	11.0
Lymphocytes, large	1.0
Monocytes	18.5

The red blood-cells varied in size and showed some loss in color. The blood-platelets were increased in number.

One month later the patient had improved markedly. Beneficial effects of the irradiation were immediate. The weakness and fatigability had lessened and the dyspnea had almost disappeared. His restlessness and tremor were much less. The prominence of his eyes was less marked and no thyroid enlargement was noted. The basal metabolic rate had fallen to plus 14 per cent. Blood examination revealed less anemia, but otherwise was essentially the same. In place of the large lymph-nodes in the right cervical region only a few small nodes could be felt. The small nodes in the axillary and inguinal regions remained as before. The mediastinal dulness, however, had increased and the spleen did seem larger.

The patient's condition varied but slightly in the next nine months. During these nine months he was given several treatments with radon and high voltage Roentgen rays. At the end of this time he complained again of fatigue, weakness, and loss of appetite. He had a return of dyspnea together with a slight non-productive cough. He perspired more than usual. The eyes showed some exophthalmos and a very slight lid lag. The extended tongue and fingers gave a moderately coarse tremor. His skin was quite moist and hot and a temperature elevation of 102° F. was recorded. The cervical lymph-nodes had again enlarged, the largest reaching a diameter of 4 cm. on the right side. The axillary and inguinal lymph-nodes showed no increase

in size. A basal metabolic rate determination was made, revealing a rise to plus 28 per cent., after discounting the rise attributable to temperature.

After several more Roentgen-ray treatments the patient again comes in for observation, and he states that he feels much better than three months ago. He has less shortness of breath and he feels a great deal stronger. His weight has increased 10 pounds. He suffers from heat much less and his appetite has improved. The lymph-node enlargement has again receded, the largest gland in the right cervical region measuring 2 cm. in diameter. The skin is not abnormally moist or warm and there is no clinical evidence of increased metabolic activity. The temperature is normal. His eyes show less protrusion than three months ago, and no lid lag can be demonstrated. The thyroid gland cannot be felt and there is no thrill or bruit present over the gland. Even the extremities and tongue show absence of tremor. Another basal metabolic rate determination this morning substantiated our clinical impression and this time it was well within normal limits, the variation being plus 5 per cent.

We will discuss this case after presenting the second patient.

Case II.—This patient is a Russian by birth. He is forty years of age and a bookbinder by trade. He came to this clinic twenty-two months ago complaining of "swollen glands" of one month's duration. Two years before that entry he had had itching of the skin over his chest and back. This had continued up to the time of his first visit to the hospital. During the year preceding he had felt more tired and weak than formerly, yet his duties were of such responsible and pressing nature that he often worked as much as sixteen hours per day. A month previous to his visit to this hospital he had a very mild sore throat with swelling of the lymph-nodes in his neck. These did not disappear and their persistence caused him to consult a physician. He had lost only a few pounds in weight.

The family and past histories were essentially negative. His habits were fairly regular and of no consequence except that he had slept very poorly of late.

Physical examination at that time showed the patient to be a well-developed, rather obese man, who was rather nervous and restless. There was a coarse tremor of his tongue and eyelids. The skin was dry and scaly over the chest and back, but elsewhere it was quite moist and warm. There was a yellowish-brown pigmentation over the chest and back, resembling tinea versicolor. The tonsils were quite large and a little red. The cervical lymph-nodes showed a diffuse enlargement, the individual nodes varying from 1 to 4 cm. in diameter. They were discrete, fairly soft, and not tender. In the axillæ and groins a few slightly enlarged lymph-glands could be felt. An epitrochlear gland that measured about 1 cm. in diameter was felt on either side. The chest examination revealed no variation from normal. The liver descended 1 cm. below the costal edge on deep inspiration. A Roentgen-ray examination of the chest showed no increase of the mediastinal shadow and there was no evidence of pathologic changes elsewhere in the thorax.

Blood studies gave the following results:

Hemoglobin (Sahli)	125 per cent.
Red blood-cells	5,856,000 per c.mm.
White blood-cells	62,300 per c.mm.
Differential count:	Per cent.
Polymorphonuclear neutrophils	7.0
Lymphocytes, small	90.5
Lymphocytes, large	1.5
Monocytes	1.0

The red blood-cells showed no variation in size, shape, or color from normal. The blood-platelets were approximately normal in numbers.

He was given 1000 electrostatic units of high voltage Roentgen-ray irradiation over the enlarged nodes, after which he rapidly improved a great deal symptomatically. The enlarged lymph-nodes decreased in size.

Eighteen months ago, however, he returned to the hospital, this time complaining of increasing nervousness, profuse sweating, and moderate cardiac palpitation. He had lost no weight. Examination showed an entirely new group of findings. His

skin was quite warm and very moist. The perspiration stood out in beads over his face. There was a marked, moderately fine tremor of the fingers, the tongue, and the eyelids. The eyes were a little prominent and a definite lid lag was demonstrable. The thyroid gland did not appear enlarged, nor could any enlargement be felt upon examination. The superficial lymph-nodes were again enlarged, especially in the cervical region, where the largest glands measured 2 cm. in diameter. The liver and spleen were somewhat enlarged. The basal metabolic rate was determined and an increase to plus 34 per cent. was found. Treatment with Roentgen rays was again resorted to, with a disappearance, in a few weeks, of the tremor, profuse sweating, and nervousness. The lymph-nodes again decreased in size. The basal metabolic rate had dropped to minus 1 per cent. about two weeks after irradiation.

For the past eighteen months the patient has returned to the clinic at regular intervals, and from time to time has had a return of his symptoms, followed by relief after irradiation.

Three days ago he again returned to the hospital with an acute upper respiratory infection and a fever of 102° F. With rest in bed and proper treatment this infection rapidly improved and for two days he has now had a normal temperature. He is now unduly restless and he is moving about continuously in bed. His respirations are increased to 24 per minute. There is a rather marked fine tremor of his fingers and tongue, and you may note that his eyelids show a continuous twitching. His skin is very moist and the perspiration runs off his face in spite of the temperature of the room, which is only 72° F. His eyes are rather prominent, yet no lid lag can be made out. The thyroid gland is soft and easily felt, but there is no thrill or bruit present over the gland. The lymph-nodes on both sides of the neck are enlarged, the largest being on the left side, measuring about 2 cm. in diameter. In the axillary and inguinal regions the lymph-nodes are smaller and they are soft and easily separated from one another. The chest examination at present is essentially negative. Examination of the abdomen reveals a large spleen reaching 3 cm. below the costal margin. The liver

descends 2 cm. below the edge of the ribs on deep inspiration. Basal metabolic rate determinations have been made today and yesterday, and elevations of plus 57 and plus 59 per cent. have been found. The basal pulse rate has averaged 84 beats per minute.

DISCUSSION

You will see that these 2 cases have several abnormalities in common, which are also found in hyperthyroidism. They are types of lymphatic tissue disease, the first being Hodgkin's disease, while the latter is a case of lymphatic leukemia. In the first case there was weakness, fatigue, increased respiration, excessive sweating, a rapid pulse rate, and a very warm and moist skin. The second case exhibited a similar state, with excessive fatigue. These are symptoms of increased metabolic activity. A second group of disorders were present, and these were very similar to those found in exophthalmic goiter, namely, a marked tremor of the tongue and fingers, a fulness of the thyroid region, slight exophthalmos, and lid lag. These signs occurred especially when disease of the lymphatic tissue had become particularly active. In exophthalmic goiter there is generally an exophthalmos associated with lid lag and inability to properly converge the eyes. The latter sign has not been present in these cases, and the degree of exophthalmos was never as marked as is often found in exophthalmic goiter. The thyroid gland was always soft in consistency and a thrill or bruit was never made out in contrast to what is usually found in Graves' disease.

The treatment of hyperthyroidism is usually by surgical methods or by irradiation with Roentgen rays of the thyroid area. In these 2 cases treatment by irradiation alone was resorted to and this was given either over the spleen, thorax, or enlarged lymph-nodes. This always caused a fairly prompt regression of the exophthalmos and tremor. The symptoms of hypermetabolism decreased and the basal metabolism always dropped after such treatments. It is interesting to speculate what changes could be produced in the symptoms of increased metabolic activity if Lugol's or some other form of iodin solution

was given in such cases as these with exophthalmos and thyroid enlargement. Lugol's solution has been given a few patients with chronic leukemia, but no decrease in the basal metabolism or change in the condition of the patient took place. In these cases, however, no exophthalmos or thyroid enlargement was recorded.

The question naturally arises as to why the exophthalmos and thyroid enlargement should occur in cases of lymphoblastoma. It is possible that the thyroid gland is somewhat involved in the disease process since there is lymphatic tissue in and around this organ. In differentiating exophthalmic goiter from lymphoblastoma with symptoms and signs of the sort these 2 patients have shown it is important to recognize that there is a much greater degree of exophthalmos and thyroid enlargement, as well as a much firmer consistency of the thyroid gland in the former than in the latter. In lymphatic tissue disease the enlargement of the lymph-nodes and often the spleen and liver together with a study of the blood-picture will, of course, give a direct clue to the primary condition present.

CLINIC OF DR. JOSEPH T. WEARN

FROM THE FOURTH MEDICAL SERVICE OF THE BOSTON CITY HOSPITAL

THE VALUE OF RENAL FUNCTION TESTS IN THE DIAGNOSIS OF EARLY NEPHRITIS

THE introduction into medicine of the more exact diagnostic procedures and tests has contributed to the accuracy of diagnosis, but nevertheless care must be exercised to insure their proper use and understanding. In a teaching hospital, for instance, one is likely to find a very frequent use made of the electrocardiograph, the *x*-ray, and numerous renal function tests; and unless one understands that the procedures are employed in many instances for teaching—to confirm or serve as a check upon the physical findings—he may get the impression that they are used too freely and that too much dependence is being placed upon them. This, of course, is erroneous, for the object of the liberal use of these methods of diagnosis is to train the student in such manner that he can recognize the value of the tests, and hence employ them intelligently when in practice and in such a way that they serve him and aid in reaching the best understanding of the patient's condition. Anyone, for example, who has made the diagnosis of auricular fibrillation by auscultation and has had his findings repeatedly confirmed by electrocardiographic studies should have more and not less confidence in his ability to recognize the condition by auscultation alone.

A thorough understanding of a test, of course, leads to intelligent use of it, and this is particularly true of tests devised for measuring kidney function. It might be profitable, therefore, in the light of more recent advances in the physiology of the kidney to examine the more common function tests, to find out what they actually measure and the degree of their delicacy.

All of the recent findings in the study of renal physiology cannot be transferred *in toto* to man, but many of the new facts make the interpretation of the results of function tests clearer and simpler.

Some years ago Cushny[1] propounded the so-called "Modern Theory" of urine formation. This he did after a careful study of all the existing literature. The theory, in brief, postulates filtration through the glomerulus and reabsorption in the tubules. The reports from the laboratory of A. N. Richards[2, 3, 4, 5] have thrown new light upon the function and behavior of the glomeruli and tubules, and as a result of this work and of the confirmatory findings of White and Schmitt[6] and others some form of filtration through the glomeruli with reabsorption in the tubules is now well established. The fluid which passed through the glomerulus was found to be free from protein, but contained sugar and chlorids in concentrations very close to that of the blood, while the bladder urine was sugar free and contained scarcely a trace of chlorid.

It was further demonstrated that various dyes, including phenolsulphonephthalein, passed through the glomeruli. It is no longer necessary, therefore, to invoke the mysterious force of secretion to explain the elimination of the dyes. Cushny's theory is now supported by facts.

Of equal importance as an aid in understanding kidney function tests were Richards' observations of the behavior of the circulation in the glomerular capillaries. In the living frog's kidney he observed the circulation in the glomeruli, the intermittence of blood flow through them, and how a single capillary loop opened in one glomerulus to permit a rapid flow of blood with the corpuscles in single file, while a nearby glomerulus opened all its loops widely to permit a lazy circulation with corpuscles two abreast. Of striking interest and of great import was the observation that few of the glomeruli were at work at any one time, but a large reserve remained inactive. Diuretics, urea, salt, glucose, or water brought many new ones into play and the ones already at work would excrete urine so rapidly that the capsules of Bowman were distended and stood out as tense little

blisters on the surface of the frog's kidney. The bladder likewise filled at a surprisingly rapid rate, but never did these substances succeed in getting all the glomeruli to work at one given time. As a result it is now possible to look upon the kidney not as an individual organ functioning as such, but as an organ made up of a group of units, each unit being a glomerulus with its tubule. Moreover, the kidney has only enough units in action at any given time to do the work required of it, thus keeping at all times a reserve of units.

With these facts in mind an understanding of the object of the more common tests for measuring renal function makes it possible to place them in the two following general groups: (1) Tests which are designed to measure the output of a substance in a given time, but which do not throw additional work or a strain upon the kidney. Into this group fall the phenolsulphonephthalein test and the lactose and iodid tests. (2) The second group includes those procedures which test the ability of the kidney to respond to sudden strain. Several ways have been devised for creating the strain, but the point in common is to increase those foods in the diet—protein, salt, and fluid—all of which the kidney excretes, and in this way add to the load. A brief mention of some of these tests is not amiss, as it may serve to illustrate the various methods of producing the added load.

The water excretion test of Volhard[7] is one of the more reliable tests and depends upon the response of the kidneys after drinking 1500 c.c. of water. It is employed more extensively in Germany than in this country, although Pratt's test[8] is a modification of it. It is a simple test to carry out and its interpretation offers no difficulties.

MacLean[9] has produced the strain on the renal function in his test after giving 15 gm. urea by mouth. He then determined the percentage of urea in the urine collected in two or three hourly periods after the dose has been given. Addis[10] has succeeded in producing even greater strain by giving larger doses of urea (30 gm.) in a liter of water, and following this with 2 glasses of water per hour for three or four hours. By deter-

mining the urea in the blood and in the hourly specimen of urine he claims to measure the amount of secreting tissue. His claim would hold only when the strain is great enough to call into full activity all the secreting tissue. Fortunately, the value of the test is not disturbed by the author's assumption of secretion. The stimulants and depressants which he warns against have been shown to influence the rate of filtration through the glomeruli. Addis and Shevky[11] have brought about strain also by omitting fluids from the diet for twenty-four hours and determining the concentration of the urine by means of the specific gravity. In the average normal subject the specific gravity is in the region of 1.032, but a low intake of food may give a lower figure.

Finally the well-known concentration test of Hedinger and Schlayer with its modifications by Mosenthal and Christian employs an increased amount of salt, protein, and fluid at mealtimes, and measures the response by determination of the volume, specific gravity, salt and nitrogen of the urine collected at two hourly intervals during the day, and of the entire night volume. In the common use of the test the salt and nitrogen are not determined, as these figures add very little to the information given by the figures of the volume and specific gravity.

There are, of course, numerous modifications of these procedures, but, as a rule, they offer no great improvement over the ones mentioned. It is obvious then that the first group of tests will not be a measure of the reserve units, while the second group theoretically should measure a decrease in reserve units provided the load thrown upon the kidney is great enough to call all of them into play. Fortunately for man and unfortunately for the success of these tests the number of reserve renal units is tremendous and can handle all strains thrown upon the normal kidney efficiently and without delay.

It is well known that disease of the kidney can actually destroy the units and so reduce their number, or it can so alter the units—either the glomerulus or the tubule, or both—that their efficiency is decreased. Also there may be both diminished

efficiency of the individual glomerulus and a reduction in the total number.

Efforts have been made in devising function tests to have them detect any diminution in function, and the delicacy of a test, of course, depends upon its efficiency in detecting such a decrease in the function of the units. In the two-hour renal test, for instance, a strain is thrown upon the kidney in the middle of the day, and in normal individuals the kidneys promptly take care of the added salt, nitrogen, and water. This can be illustrated if it is assumed that in order to excrete the basal amount of urine each day a normal kidney uses X units. If, however, a heavy meal containing large amounts of salt, protein, and water is given, the kidney, in order to prevent an increase in salt, urea, and water in the blood, calls into play two X units. Hence in the two-hour test in a normal man the volume and specific gravity of the urine may increase after a meal. It is even possible that a normal person may have a total of 5X units, in which case the strain produced by the two-hour test-meal requiring only 2X units would not employ the 3X reserve units. If, on the other hand, the kidney has been damaged and less than X units remain, it will not be able to excrete the added water, salt, etc., immediately, and the volume and gravity would show fixation, because the remaining units working at maximum efficiency can put out only a given amount of urine per hour, and each hour's output therefore would be approximately the same. They continue this rate of work until the concentration of salt and nitrogen in the blood is brought to a normal level, and this often requires their working into the night, which, of course, results in a high night volume of urine.

To measure the earliest diminution in renal function, therefore, the test must detect the decrease in function of the reserve units.

Inasmuch as the phenolsulphonephthalein test does not place any great strain upon the kidney, it would not in any way measure the reserve units. Consequently one does not expect any reduction in the output of this dye until the kidney is greatly damaged, or until the reserve units have been destroyed.

Foster[12] has recently submitted some of the tests to trial in patients with one kidney. This amounts to a crucial experiment in determining the value of function tests clinically, for in the absence of one entire kidney the reserve units are greatly diminished. With this in mind Foster observed the functional response of these patients to the concentration and urea ratio tests of Addis and to the water excretion test of Volhard. All of these tests throw greater strain upon the kidney than the concentration tests of Mosenthal and Christian, and are, therefore, to be considered as more delicate tests.

The urea ratio test of Addis showed slight change in all the patients within three weeks after the removal of one kidney, but the other tests while showing slight change in some gave normal results in others. The results are best shown in the following from Foster's paper: "The decrease in renal tissue in a person with one kidney is only doubtfully revealed by these tests when the findings are compared with those of a normal subject." The phenolsulphonephthalein test and the blood nitrogen were normal in all the patients, and it is safe to assume that the lactose and iodid tests are no more delicate than the phenolsulphonephthalein test.

The most delicate tests that can be employed at the present time in determining renal function, therefore, begin to detect changes when kidney function has been reduced by 50 per cent. or by the removal of one kidney. This does not mean that the tests are of no value, for at times they are of great assistance in determining the amount of kidney damage in more advanced cases and hence are of definite value in prognosis and treatment.

In this discussion attention has been directed chiefly toward the delicacy of the tests for measuring renal function and nothing has been said concerning their accuracy. The well-known variation in the output of phenolsulphonephthalein when that test is repeated in the same subject from day to day, is a good example of inaccuracy. If, on the other hand, approximately 66 per cent. or more of the kidney tissue is removed, the output of the dye begins to diminish and fall rather constantly below 40 per cent.

Similarly, the urea ratio of Addis begins to detect a diminution of renal function when approximately 50 per cent. of the functioning tissue is destroyed. But this very fact shows that the strain imposed upon the kidney by this test is not sufficient to call into play all the urea- or water-excreting units, hence when a patient has 75 per cent. of his kidney function intact it is reasonable to expect variations in this test from day to day. It might be said that the end point of the reaction is qualitative rather than quantitative when it fails to detect the presence of damage to 50 per cent. of the function.

These results also enable one to understand the value of blood nitrogen, uric acid and creatinin determinations, which have been employed so freely in many instances where they could not possibly throw light upon the patient's condition.

If one considers the fact that the blood nitrogen increases only after the units have been so reduced in function that they cannot keep pace with the protein intake in the diet—in other words, in advanced kidney damage and generally after the specific gravity has become fixed—it becomes clear that this determination is of value in regulating the amount of protein in the diet. The injured units are able to eliminate urea and other nitrogenous end products from the blood and keep them at a normal level only so long as the rate of intake of protein does not exceed the rate of output. This statement is rather sweeping and is not meant to cover conditions other than nephritis. In this disease it is of value in diagnosis particularly as an aid in determining how far advanced the disease is.

Other studies made recently have shown that red blood-cells occur in normal urine, and can be found in freshly passed specimens. This finding has long been considered evidence of renal damage and much dependence has been placed upon it as a sign of pathology in the kidney. In addition to this it is now known that albumin is present in the urine of normal men following exercise, excitement, and in several other conditions in the absence of kidney disease. Each of these findings, while increasing knowledge of the kidney, adds a new guide-post to the correct diagnosis of early nephritis. They teach the proper value to be

placed upon the finding of albumin in the urine; and warn that the presence of a few red blood-cells alone is of no significance.

These statements seem to smack of pessimism, but such is certainly not their intention. Analysis of the most delicate renal function tests indicates that, while they are an improvement over older tests, they still do not furnish great assistance in detecting early damage to kidney function. They do hold out the hope, however, that more study might reveal a way of placing sufficient strain upon a kidney to discover the earliest changes in its function.

Such a consideration of methods also shows the advisability of employing the history, physical examination, and all known means along with the function tests rather than depending upon the tests alone.

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CLINIC OF DRS. ELLIOTT P. JOSLIN, HOWARD F. ROOT, AND PRISCILLA WHITE

NEW ENGLAND DEACONESS HOSPITAL

DIABETIC COMA AND ITS TREATMENT

Introduction.—Coma and cancer each caused 6 deaths among the 1138 diabetic patients seen during the year ending July 1, 1926. Albeit coma has lost its priority in diabetic mortality, it is still a serious complication. It merits another clinic, because it is common and treatment can be successful. It would almost seem as if children throve on coma. Forty-five of our living group of 200 or more children have already had coma 53 times, in 9 of the number diabetes was discovered during coma, and yet during the year mentioned above not one of the deaths from coma occurred in a patient under fifteen years of age. Coma today is as dangerous as ever, but is far less fatal, in fact but 10 per cent. of the fatalities last year were due to coma. For this improvement in treatment all are thankful, but it is not enough. Coma should be rendered far less frequent by emphasizing prevention because it is preventable. Each diabetic patient and each family of a diabetic should be taught that coma is avoidable and how to avoid it. We believe that coma was preventable in the 30 successive cases which form the basis of this clinic and hence the 4 fatalities were all the more distressing, just as were the 2 fatalities in our preceding series of 33 cases.[1, 2]

The number of cases of coma would have been far larger had not the physicians who refer cases to us acquired the excellent habit of promptly beginning treatment of the coma case in the

[1] Joslin, Root, White: Med. Clinics North America, 1925, 8, 1873.

[2] Joslin, Root, White, Kiefer: Med. Clinics North America, 1925, 8, 1921.

home. By this means many cases just coming out of coma or just on the verge of coma enter the hospital and yet fail to show a CO_2 combining power of the blood-plasma below 20 volumes per cent., the arbitrary dividing line of coma in our series. Then, too, many physicians of our old patients consult us about coma cases by telephone. In this way one learns how many cases of coma are being saved in the community. If a doctor far from a laboratory is willing to stay up all night working over a coma case, the least one can do is to be willing to have him telephone every hour or two for an exchange of ideas. Thus far we have had only one radio call, but that was from the middle of the Atlantic Ocean. The physician hesitated to give insulin because the patient did not eat, the advice to give the drug very frequently in somewhat reduced doses as long as the urine contained sugar may have prevented a fatality.

Explanation of Frequency of Coma Today.—As long as a diabetic patient does not overeat he will not contract coma, will not die of coma, though he may die of inanition. He can overeat of food carelessly or overeat of his own body innocently, because in fever or in hyperthyroidism he does not realize his metabolism is raised and he is overeating. However, overeating for a diabetic is a very different proposition from overeating for a healthy man. The calories which constitute even a normal diet for a man in health represent overeating, an excessive diet, for the patient with diabetes. The only way the severest diabetics can exist is by undereating, by living on a lowered plane of metabolism. Insulin, it is true, allows the intake of a normal quantity of food, but every insulin-taking diabetic is overeating so far as his own resources are concerned, and if he omits his insulin and continues his food he will pay the penalty of the reckless and disobedient diabetic, and if a severe case he will develop coma. Furthermore, even if he stops eating and gives up insulin he may develop coma, because he no longer is the thin diabetic with a low metabolism, who can oxidize the little carbohydrate, protein, and fat which his emaciated body requires; for today he is usually well nourished and his own tissues are capable of furnishing him many hearty meals which he cannot

utilize without insulin. Therefore every insulin diabetic is overeating, and since overeating leads to coma every insulin. diabetic is a potential coma case, and consequently should be treated accordingly.

The Everyday Causes of Coma Are Preventable.—If an insulin-treated diabetic omits his insulin, he should be taught that he is in danger of coma when sugar appears in his urine, even though he curtails or omits his diet. He must be made to realize that he can overeat his own tissues and that he always requires insulin as long as sugar shows.

Irregularities of diet exceed by far any other cause of coma. A history of broken diet was obtained in 70 per cent. of our series. The girl whose first attack was precipitated by banana royal and hot dogs when she returned in her second experience had peanuts washed out of her stomach, to the edification and we hope to the future salvation of the other patients in the ward. Nausea and vomiting were actually present in 76 per cent. of 30 coma admissions at the New England Deaconess Hospital from April, 1925, to February, 1927. Though it is true the diabetic is not exempt from the conditions causing nausea and vomiting other than acidosis, such as indigestion, duodenal ulcer, acute appendicitis, gall-stones, coronary thrombosis, acute infectious diseases, any one of these conditions can and will precipitate coma. One state passes quickly into the other, each masking the other and making the end-result more serious. Unable to take food, the uneducated, unprepared diabetic patient omits his insulin and coma follows. We have been forced to conclude that in diabetes vomiting is a sign of evil omen and unless heeded leads to death.

The number of cases of coma precipitated by infections has increased, compared with the series reported in May, 1925. Of the 30 admissions for coma since May, 1925, 60 per cent. had a temperature above 99.6° F. The infections for the most part were not severe in type with the exception of 2 instances, an acute pancreatitis with fat necrosis and a carbuncle which was followed by peritonitis and septicemia. In the remainder the infections were of an upper respiratory nature, tonsillitis, and

TABLE 1

Thirty-three Consecutive Cases of Coma or Impending Coma Treated Without Alkali but With Insulin

Case No.	Age at coma, yrs.	Duration of D. M., yrs.	Date.	Clinical data.		Blood.									Urine.			Insulin.		
				Respiration.	Mental condition.	Sugar, per cent.			Plasma CO_2 combining power volumes, per cent.			Non-protein nitrogen mgm. per 100 c.c.			At entrance.		Sugar free after entrance, hours.	Units.		
						Day.			Day.			Day.			Diacetic acid.	Sugar, per cent.		Day.		
						1	2	3	1	2	3	1	2	3				1	2	3
			1923																	
1609	17.1	6.4	Dec. 7	Kussmaul.	Drowsy.	0.33	0.26	—	24	—	—	26	—	—	++++	3.0	—	60	30	40
2448	19.3	1.3	Apr. 24	Kussmaul.	Drowsy.	0.33	0.21	—	21	37	—	—	—	—	++++	5.4	192	60	30	30
2448	19.6	1.7	Aug. 11	Kussmaul.	Drowsy.	0.27[1]	0.25	—	31[1]	43	—	—	—	—	++++	3.2	34	130	50	55
2687	25.4	1.7	Aug. 28	Kussmaul.	Drowsy.	0.23	0.21	—	26	55	—	—	—	—	++++	3.8	—	75	60	60
2801	15.9	1.1	June 10	Kussmaul.	Drowsy.	0.33[2]	0.28	0.29	36 2[2]	43	17	29	—	—	++++	3.5	24	260	30	115
3021[10]	22.5	1.2	Oct. 21	Kussmaul.	Unresponsive.	0.72	—	—	12	—	—	47	—	—	+	2.8	—	80	—	—
3040	11.3	1.0	Oct. 3	Kussmaul.	Drowsy.	0.34	0.24	0.29	12	31	—	25	31	—	++++	4.0	7.5	55	30	40
3129	24.4	3.7	Dec. 30	Kussmaul.	Drowsy.	0.37	0.28	—	22	36	—	27	—	—	++++	3.8	72	90	55	55
3137	45.2	2.3	May 13	Kussmaul.	Drowsy.	0.37	—	0.16	20	—	65	32	—	—	++++	5.0	144	70	40	30
3240[11]	16.0	0.7	July 20	Kussmaul.	Stuporous.	0.49	—	—	13	—	—	—	—	—	++++	4.0	—	60	—	—
3382	28.4	3.4	Sept. 15	Kussmaul.	Unresponsive.	0.55	0.17	0.30	11	71	20	66	36	—	++++	1.8	19	160	90	80
			1924																	
2988	56.3	4.0	Apr. 21	Kussmaul.	Stuporous	0.48	0.29	—	14	49	—	49	61	—	++++	3.0	17	170	100	80
3129	25.3	4.5	Oct. 27	Kussmaul.	Stuporous.	0.46	0.27	0.36	8	19	20	37	26	—	++++	3.5	105	120	35	30
3143	17.5	1.1	Mar. 29	Kussmaul.	Stuporous.	0.50	0.26	0.24	20	29	34	50	39	—	++++	1.2	27	170	210	100
3502	14.0	1.3	Dec. 5	Kussmaul.	Drowsy.	0.40	0.09	—	16	39	—	—	29	—	++++	2.6	14	165	25	20
3666	29.0	0.8	May 11	Kussmaul.	Drowsy.	0.43[3]	0.36	—	19[3]	37	—	—	30	—	+++	3.0	20	150	110	112
3859	22.8	0.1	Mar. 26	Kussmaul.	Drowsy.	0.37	0.31	0.31	25	32	30	—	31	—	++	4.0	34	100	200	175
3877	15.3	0.7	Dec. 16	Kussmaul.	Drowsy.	0.36	—	0.17	22	—	—	—	—	—	++++	3.3	8	30	20	30
4033	46.1	0.1	July 24	Kussmaul.	Stuporous.	0.60[4]	0.29	0.36	21[4]	50	—	85	61	56	++	4.0	168	210	110	80
4109	38.8	2.6	Sept. 2	Kussmaul.	Stuporous.	0.40[9]	0.05	0.18	14	32	45	—	23	—	++++	3.5	54	240	40	30
4110	12.0	1.7	Sept. 1	Kussmaul.	Stuporous.	0.16[5]	0.19	0.31	13[5]	22	30	27	37	—	++++	1.4	5	110	20	25
4115	51.8	0.5	Aug. 21	Kussmaul.	Stuporous.	0.30	0.03	0.29	20	45	—	—	27	—	++++	3.6	22	195	30	38
4157	54.9	9.8	Oct. 1	Kussmaul.	Unresponsive.	0.63	0.06	0.43	13	24	19	61	30 3	—	++++	3.0	36	250	15	60
4171	67.0	0.9	Sept. 23	Kussmaul.	Unresponsive.	0.66	0.44	0.17	14	20	25	58	63	—	+++	3.6	30	120	110	35
4194	61.3	9.6	Oct. 31	Kussmaul.	Drowsy.	0.30	0.17	—	18	33	—	36	—	—	++++	3.0	—	65	65	—
4232	16.9	1.6	Aug. 18	Kussmaul.	Unresponsive.	0.49[6]	0.16	0.36	11[6]	22	20	53	69 1	139	+++	2.0	20	300	70	50
4271	30.3	0.4	Dec. 3	Kussmaul.	Drowsy.	—	0.13	—	16	35	—	—	22	—	+++	4.0	12	25	10	25
4279	61.2	2.3	Oct. 28	Kussmaul.	Drowsy.	0.36	0.44	0.18	24	33	48	39	—	—	++++	2.8	22	20	100	45
4289	29.4	0.1	Dec. 6	Kussmaul.	Drowsy.	0.54	0.62	0.33	11	18	32	—	—	—	++++	2.2	8	145	95	45
			1925																	
2024	15.3	4.3	Feb. 24	Kussmaul.	Emotional.	0.46	—	—	16	—	—	—	—	—	++++	3.0	—	65	—	—
2786	44.5	2.7	Mar. 8	Kussmaul.	Unresponsive.	0.59[7]	0.36	0.29	10[7]	21	24	43	—	—	++++	4.0	12	270	80	50
3391	37.3	2.4	Jan. 9	Kussmaul.	Stuporous.	0.55	0.21	0.25	15	39	37	74	69	—	++++	5.0	13	170	50	55
3877	15.4	0.8	Mar. 22	Kussmaul.	Stuporous.	0.77[8]	0.15	—	16[8]	46	—	61	38	—	+++	6.5	10	270	55	40

[1] Insulin 40 units during five hours preceding blood-sugar.
[2] Insulin 240 units during twelve hours preceding blood-sugar.
[3] Insulin 50 units during five hours preceding blood-sugar.
[4] Insulin 35 units during five hours preceding blood-sugar.
[5] Insulin 60 units during eight hours preceding blood-sugar.
[6] Insulin 30 units during two hours preceding blood-sugar.
[7] Insulin 40 units during three hours preceding blood-sugar.
[8] Insulin 60 units during three hours preceding blood-sugar.
[9] Patient given soda bicarbonate before entrance.
[10] Death three and a half hours after admission.
[11] Death six hours after admission.

TABLE 2

Thirty Consecutive Cases of Diabetic Coma or Impending Coma Treated Without Alkali, but With Insulin

Case No.	Age at Coma	Duration of D.M. yrs.	Date	Clinical Data: Respiration	Clinical Data: Mental Condition	Blood Sugar, Per Cent: 1	Blood Sugar, Per Cent: Day 2	Blood Sugar, Per Cent: Day 3	Plasma CO_2 combining power Volumes per cent: 1	Plasma CO_2: Day 2	Plasma CO_2: Day 3	Non-protein nitrogen mgm. per 100 c. c.: 1	Non-protein nitrogen: Day 2	Non-protein nitrogen: Day 3	Urine At Entrance: Diacetic Acid	Urine At Entrance: Sugar per cent	Urine: Sugar Free after entrance: Hours	Insulin Units: 1	Insulin Units: Day 2	Insulin Units: Day 3
			1925																	
4525	53.7	2.1	Apr.17	Kussmaul	Responsive	0.80	-	-	5	-	-	46	-	-	++++	3.1	-	497	-	-
3040	12.9	2.5	May 13	Hyperpnoea	Responsive	0.40	-	-	[illegible]	-	-	-	-	-	++++	4.8	29	160	60	55
4710	14.7	2.4	July10	Kussmaul	Responsive	0.45	0.13	-	15	35	-	38	29	-	++++	3.0	10	250	68	50
4763	16.3	0.1	Aug.17	Kussmaul	Responsive	0.36	0.27	-	19	34	-	-	-	-	+++	1.4	-	60	40	40
3129	26.2	5.5	Oct.30	Kussmaul	Unrespon.	0.78	-	-	15	-	-	58	-	-	++++	4.0	14	295	65	45
4224	11.0	0.9	Sept.15	Kussmaul	Unconscious	0.40	0.04	0.26	10	25	23	42	37	53	++++	5.5	16	170	45	25
4766	15.9	0.1	Aug.23		Responsive	0.29	-	0.31	17	-	32	-	-	-	+++	3.5	6	50	40	40
3267	43.0	3.0	Sept.25	Kussmaul	Responsive	0.44	0.23	-	8	14	-	98	81	-	+	0.3	13	240	-	-
3006	18.9	3.3	Aug.26	Kussmaul	Unrespon.	0.72	0.35	-	12	29	-	48	56	-	++++	5.0	21	260	35	30
3739	14.2	1.8	Dec.15	Kussmaul	Delerium	0.29	0.27	0.16	12	17	-	34	-	-	++++	3.4	13	170	106	87
			1926																	
5065	58.5	5.7	Jan.29	Kussmaul	Responsive	0.60	0.12	-	15	35	-	66	35	-	0	4.0	12	120	35	40
3456	41.5	3.0	Jan.28	Kussmaul	Responsive	0.76	0.10	0.17	19	-	56	68	51	-	++++	5.0	11	160	90	60
5187	63.7	2.1	Feb.22	Kussmaul	Responsive	0.72	0.35	-	14	30	-	74	54	-	++	3.5	13	350	165	160
5176	45.0	2.6	Apr.13	Kussmaul	Unrespon.	0.67	0.46	0.26	12	10	40	67	80	68	++	1.0	32	216	175	95
3040	13.9	3.5	Mar.18	Kussmaul	Responsive	0.56	0.10	-	19	44	-	40	-	-	++++	3.8	5	105	75	45
3877	16.7	2.2	July 1	Kussmaul	Responsive	0.40	-	-	10	-	-	29	-	-	+++	1.5	9	165	60	35
5458	3.8	0	Aug.18	Kussmaul	Responsive	0.30	-	-	20	-	-	-	-	-	++++	6.0	27	16	12	12
3877	16.9	2.3	Aug.12	Kussmaul	Responsive	0.20	-	0.35	20	-	32	-	-	-	+++	0.3	13	55	45	45
4740	35.5	2.4	Sept.9	Kussmaul	Responsive	0.40	0.29	0.25	13	32	46	-	31	-	++++	4.5	9	150	35	40
2982	55.1	19.2	Sept.30	Normal	Responsive	0.51	0.18	-	20	34	-	33	-	-	0	3.5	-	130	35	45
4978	18.1	2.2	Sept.12	Kussmaul	Unconscious	0.49	0.43	0.24	9	16	26	41	72	106	+++	2.0	48	235	100	20
5632	34.6	0	Oct.31	Kussmaul	Unconscious	0.80	0.21	0.25	12	30	26	-	74	-	++	5.5	19	250	30	55
4232	19.1	3.7	Oct.25	Kussmaul	Responsive	0.29	0.24	-	17	26	-	36	-	-	++++	4.2	6	105	70	50
2797	15.7	5.8	Oct.3	Kussmaul	Responsive	0.29	0.06	-	19	41	-	-	22	-	++++	4.5	10	65	45	30
3677	17.1	2.5	Oct.28	Kussmaul	Responsive	0.29	-	-	18	-	-	34	-	-	++++	3.8	5	90	50	50
3682	12.7	4.0	Nov.1	Kussmaul	Responsive	0.33	0.34	0.28	13	16	16	35	-	-	++++	2.1	9	73	40	65
4535	39.2	1.9	Nov.8	Kussmaul	Responsive	0.53	-	0.27	8	-	23	27	-	--	+++	3.0	-	130	45	65
			1927																	
5784	54.4	0.1	Jan.14	Kussmaul	Responsive	0.53	0.12	-	16	39	-	28	27	-	++++	3.0	5	80	25	25
5121	34.3	0.9	Jan.12	Kussmaul	Responsive	0.66	0.12	0.26	12	40	-	45	-	-	++++	5.0	8	205	45	35
4723	12.8	0.5	Feb.28	Kussmaul	Responsive	0.56	0.10	0.20	12	35	42	31	40	47	++++	4.5	18	125	35	35
Average																		166	60	49

1. Alveolar air 18
2. 2 Hours after 50 units of insulin

[illegible] Insulin 60 units during eight hours preceding blood-sugar.
[illegible] Insulin 30 units during two hours preceding blood-sugar.
[illegible] Death six hours after admission.

otitis media. In not a single case had the patient been adhering both to a regular schedule of diet and insulin. This is why a diabetic adult should report to his doctor every three months and if a child every month.

Four of the cases had been untreated, and 1 had been fasted prior to the onset of his coma.

The slow onset of coma allows time to check it. In this series the symptoms preceded the onset by more than twenty-four hours in every instance, notwithstanding the presence of an overwhelming infection in 2 of the cases and in 1 case a thyroid storm.

Patients Prone to Coma.—Coma attacks the young diabetic and the diabetic who is in the first few years of his disease. In our first series of 33 consecutive cases of coma treated in the Deaconess Hospital with insulin, Table 1, more than one-third were below twenty years of age, and in the present series, Table 2, nearly two-thirds. Fifty-three per cent. between ten and twenty years of age. These figures apply to the cases treated in the hospital. The distribution according to the age of the 122 fatal cases of coma among the 609 deaths in diabetes since the introduction of insulin is shown in Table 3.

TABLE 3

AGE DISTRIBUTION OF ALL DEATHS FROM COMA IN AUTHORS' SERIES, AUGUST, 1922 TO JULY, 1926

Age at death by decades.	Coma.	
	Cases.	Per cent.
0– 9	7	5.7
10–19	20	16.4
20–29	19	15.6
30–39	17	13.9
40–49	11	9.0
50–59	22	18.1
60–69	17	13.9
70–79	9	7.4
	122	100.0

Coma has been no respector of age, so far as our total statistics go, because the number of deaths was almost the same in the first and eighth decades. However, 52 per cent. of the total deaths were in the first four decades as compared with 63 per

cent. of 63 cases in our Deaconess Hospital series being in the first two decades. A better realization of the far greater frequency of coma in the early years of life is obtained by comparing these high percentages with the low percentages of diabetics whose disease begins under forty years. This was 33.7 per cent. for our 5400 cases. The high percentage of deaths from coma in the sixth decade is explained by the years fifty

TABLE 4

DURATION OF DIABETES AND ITS RELATION TO DEATHS FROM COMA SINCE THE ADVENT OF INSULIN

Duration of diabetes, year.	Coma.	
	Cases.	Per cent.
0– 1	8	6.6
1– 2	20	16.4
2– 3	24	19.7
3– 4	16	13.1
4– 5	7	5.7
5– 6	6	5.0
6– 7	3	2.5
7– 8	10	8.2
8– 9	8	6.6
9–10	3	2.5
10–11	5	4.1
11–12	1	0.8
12–13	2	1.6
13–14	2	1.6
14–15	2	1.6
15–16	1	0.8
17–18	1	0.8
19–20	2	1.6
20–21	1	0.8

and fifty-one, which are the peak years for onset of diabetes in women and men respectively.

More than half of all the deaths from coma take place during the first four years of the disease. This is the period, therefore, upon which all should concentrate their efforts in attempting to overcome coma. Coma is exceptional after ten years of dia-

betes. Among the 63 hospital cases, Tables 1 and 2, there was one over this duration and among the 122 coma cases since insulin there were reported but 12 cases or 10 per cent. of the total deaths from coma. In none of Petrén's[1] series of 28 comas in 25 patients was the duration of the disease over four years, and, in fact, all but 8 of his cases were under a year's duration.

The first four years of diabetes are the best hunting grounds for lowering mortality in diabetes, because here coma is most frequent and coma is the most easily preventable of all the causes of death in diabetes. Consider, for instance, the difficulty of making headway against that still more common cause of death in diabetes, namely, arteriosclerosis.

Pessimists will explain the low mortality from coma after five years of diabetes on the ground that there are few severe diabetics living at the end of five years; optimists, and we belong to this group, ascribe the low mortality to the diabetes becoming milder with age and to a better understanding of his disease on the part of the patient. This latter feature is supported by the fact that the only cases of coma treated at the hospital during the first year of the disease were previously untreated diabetics, as well as by the previous statement that with 9 children the diagnosis was first made with the patient in coma.

There is another explanation for the second, third, and fourth years of diabetes being the danger zone for diabetic coma today. One of the children says that in the first year of diabetes pride is taken in keeping to the diet, but later self control is gone. With time both pride and fear of danger are lost, until they are regained by the experience of a coma attack.

The mild diabetic is not immune to coma. One man who had an amputation of a leg at the hospital at sixty-two years of age, Case No. 5126, left the New England Deaconess Hospital for his home in the country with a diet of carbohydrate 113 grams and no insulin. One month after discharge we learned that he had died of true diabetic coma. Approximately one-third of the cases recorded in Table 2 had a carbohydrate tolerance between 80 and 100 grams with comparatively small doses of insulin.

[1] Petrén: Ergeb. d. inn. Med. u. Kinderheilk., 1925, 28, 92.

TABLE 5

Prognosis After Coma.

Case No.	Entrance Date	Condition: Alive — Date Year Mo.	Condition: Dead — Date	Condition: Dead — Cause	Condition: Dead — Days after recovery from coma.
	1923				
1609	12-- 7--23	1927 Feb.			
2446	4--24--23	1926 Dec.			
2448	8--11--23	1926 Dec.			
2687	8--28--23	1926 Apr.			
2801	6--10--23		8--16--23[1]	Coma	2 mos.
3021	10--21--23		10--21--23	Coma	
3040	10-- 3--23	1927 Jan.			
3129	12--30--23	1926 Oct.			
3137	5--13--23	1927 Jan.			
3240	7--20--23		7--21--23	Coma	
3382	9--15--23	1926 Nov.			
	1924				
2988	4--21--24		4--27--24	Pneumonia pericarditis	6 days
3129	10--27--24	1926 Oct.			
3143	3--29--24		11-- --26	Pulmonary tuberculosis	1.7 years
3502	12-- 5--24	1926 Feb.			
3600	5--11--24	1926 July			
3659	3--26--24	1927 Feb.			
3877	12--1--24	1926 Nov.			
4033	7--24--24	1926 July			
4109	9-- 2--24	1926 July			
4110	9-- 1--24	1926 Oct.			
4115	8--21--24	1926 July			
4157	10-- 1--24		10--10--24	Chronic myocarditis	8 days
4171	9--23--24	1926 Mar.			
4194	10--31--24		11-- 8--24[2]	Gangrene	7 days
4232	8--18--24	1927 Feb.			
4271	12-- 3--24	1926 July			
4279	10--28--24	1926 July			
4289	12-- 6--24		12--26--24	Septicemia	21 days
	1925				
2024	2--24--25	1926 Oct.			
2786	3-- 8--25	1927 Feb.			
3006	8--26--25	1926 July			
3040	5--13--25	1927 Jan.			
3129	10--30--25	1926 Oct.			
3267	9--29--25		9--27--25	Infecticus pancreatitis	2 days
3391	1-- 9--25	1927 Mar.			
3739	12--15--25	1927 Feb.			
3877	3--22--25	1926 Nov.			
4224	9--10--25	1927 Jan.			
4525	4--17--25		4--18--25	Peritonitis Septicemia	
4710	7--10--25	1926 Sept.			
4763	8--17--25	1926 Nov.			
4766	8--23--25	1926 Mar.			
	1926				
2797	10-- 3--26	1927 Feb.			
2982	9--30--26	1926 Dec.			
3040	5--18--26	1927 Jan.			
3456	1--28--26	1926 July			
3682	11-- 1--26	1926 Nov.			
3877	7-- 1--26	1926 Nov.			
3877	8--12--26	1926 Nov.			
3877	10--28--26	1926 Nov.			
4232	10--25--26	1927 Feb.			
4535	11-- 8--26	1926 Dec.			
4740	9-- 9--26	1927 Feb.			
4978	9--12--26	1927 Mar.			
5065	1--29--26	1927 Jan			
5170	4--10--26		4--21--26	Pulmonary infarct Empyema Thyroid storm	7 days
5187	2--22--26	1926 June			
5458	8--18--26	1926 Sept.			
5632	10--31--26	1926 Nov.			
	1927				
4723	2--28--27	1927 Mar.			
5121	1--12--27	1927 Feb.			
5784	1--14--27		1--27--27	Alkalosis--tetany	13 days

[1]Not in hospital.

[2]Refused operation and left hospital against advice.

The remainder averaged 60 to 80 grams, one of these with no insulin, so that it can be said that 80 per cent. of our coma cases treated in the hospital since 1925 were relatively mild diabetics.

Six of the 58 patients in the combined series, whose attacks of coma numbered 63 in all, died in the hospital, and we have learned of 6 other deaths since discharge, one each from coma, pneumonia, pulmonary tuberculosis, myocarditis, gangrene, and septicemia. The remaining 46 cases are alive at varying periods from four years to a few weeks since the outbreak of coma. There is little doubt that the duration of life of these cases since their coma will exceed the total duration of life of the average diabetic, 4.8 years, following the onset of his disease up to the year 1914. It is still the poorer class of patients in whom the incidence of coma is highest.

Symptoms and Signs of Coma.—Nausea, vomiting, hyperpnea, drowsiness (or coma), hyperglycemia, and ketonuria and ketonemia are the cardinal symptoms and signs of diabetic coma. Added to these are vague pains in any part of the body, and useful in diagnosis is the history of irregularity in diet or insulin, of an infection or of an increase in metabolism.

The frequency of nausea and vomiting we have already stressed. Their significance we cannot overemphasize. Hyperpnea usually follows the vomiting. Kussmaul breathing is the most significant clinical finding. It was constant in 29 of the 30 cases. The exceptional patient who broke the rule had a blood CO_2 under 20 volumes per cent. without Kussmaul respiration or acetonuria. The absence of acetonuria might be explained on the ground of renal pathology, a paranephric abscess and a chronic nephritis.

Coma, complete unconsciousness, was present in 6 cases. The others could be roused in spite of the fact that the CO_2 was below 20 volumes per cent. in all, and below 15 volumes per cent. in half of the cases.

Glycosuria as pointed out by Dr. H. F. Root was not excessive. One case had a nearly sugar-free specimen on admission, due to the fact that she was a repeated offender and had taken large doses of insulin just prior to admission. Usually there

are several patients in the hospital who have shown at the time of their entrance 6 to 10 per cent. of sugar in the urine. These are not the patients whom one sees in coma. The highest percentage of sugar in this coma series was 6 per cent. Only 6 had 5 per cent. or over. Twenty-four of the patients had a glycosuria which was less than 5 per cent.

The concentration of salt and nitrogen in the urine is also low in coma and rises with recovery. This was noted years ago by Magnus Levy and Joslin. Peters and Bulger[1] found that the blood, on the other hand, was concentrated by dehydration in coma, but became more diluted with recovery.

The demonstration of acetone or diacetic acid is almost a requisite for a diagnosis. However it was not present in 2 of these cases. One has already been described. In the other no specimen of urine was obtained until the patient had received vigorous treatment for several hours.

Hyperglycemia.—High blood-sugars were associated with the severer complications. A high level of the blood-sugar is not necessarily equalled by a low level for the CO_2 combining power. The two vary greatly with the duration of the coma, and of course with the extent of treatment previous to admission. The range of blood-sugar when the CO_2 was below 20 volumes per cent. was 0.20 to 0.80. The highest blood-sugar with the patient conscious was 0.80. The lowest value for CO_2 combining power in association with a conscious patient was 5 volumes per cent.

Conditions Confusing the Picture of Coma.—The systems of the body as a whole must be expected to show changes with so sudden a disturbance in chemical equilibrium as occurs in diabetic coma. In nearly all cases there is some condition to cause anxiety in the mind of the examiner. Foremost among these are the gastro-intestinal symptoms and complications.

Gastro-intestinal.—Gastric symptoms are constant. Abdominal findings are frequent. Four patients, Case Nos. 3129, 4224, 5630, 4710, all had surgical consultations because of abdominal tenderness and muscular spasms in the presence of abdominal pain, nausea, and vomiting. Case No. 2982 had an

[1] Peters and Bulger, Arch. Int. Med., 1925, 36, 868.

abdominal operation, with negative abdominal findings. Case No. 4740 was a problem for several days. The diagnosis of acute gall-bladder was made when coma was impending. With recovery from coma his signs and symptoms disappeared entirely. As all these patients had fever and leukocytosis a differential diagnosis was extremely difficult. In spite of our findings, however, we believe that even though coma is present, if a surgeon feels reasonably sure that the patient has an acute lesion in the abdomen, operation is the safer procedure, because an acute abdominal infection may precipitate coma in the diabetic.

Explanation for the gastro-intestinal symptoms are difficult. Dilated stomachs, even with evidence of hemorrhage, would not give just the picture one so commonly encounters. Moreover, a dilated stomach was absent in some of this group in whom abdominal symptoms were present.

Pancreatitis should be considered because of the occurrence of pain in the upper left quadrant of the abdomen. But there is little clinically to suggest it. These cases do not have pancreatic stools. It is true that 1 of the 4 cases which came to autopsy showed an acute pancreatitis. We feel confident, however, that this was the cause rather than the result of the coma.

Circulatory.—A poor peripheral circulation characterizes nearly all advanced cases. Low blood-pressure and tachycardia were common. In 65 per cent. of the patients the pulse rate was 130 or above.

There is some evidence of disorderly heart action in the coma cases of this group and the April, 1925, group. Auricular flutter occurred in Case No. 4306; age at coma thirty six years; auricular fibrillation in Case No. 5176, age at coma forty-three years; heart-block in severe acidosis, not quite coma, in Case No. 1794, at thirty-three years; and alternation in Case 4157, age at coma fifty-four years.

Clinical signs of dilatation such as temporary extension of the borders beyond normal limits with murmurs and irregularities were not infrequent.

Renal.—The rôle played by the kidney is important in coma both during the actual attack and also during the days immedi-

ately following it. Casts, red cells, traces of albumin are nearly constant, oliguria frequent, and anuria occasionally occurs as it did in 3 of our cases.

Warburg,[1] in an admirable historical description of coma, includes cases without diacetic acid in which the renal deficiency brought on by acidosis was the chief factor. He noted that insulin treatment diminished the renal irritation.

The correlation of the high non-protein nitrogen values with diabetic coma does not appear difficult to explain, because of the large quantities of acid and salts which are excreted by the kidney and may result in its impaired efficiency. A rise above 40 mgm. occurred in 14 out of 25 cases. The non-protein nitrogen did not always fall in proportion to the degree of recovery from coma. High values persisted on the second and even on the third day. Case No. 4978 had symptoms of uremia on the third day. In general the severer the case and the more prolonged the coma, the higher the non-protein nitrogen.

Then, too, in these patients with a late developing high non-protein nitrogen in the blood the values for CO_2 in the plasma are low and remain low for a longer period than usual. One must certainly bear in mind, therefore, the possibility of other acid factors being present as emphasized by Starr and Fitz[2] and by Arlie Bock. Improvement in these cases, however, is not dependent exclusively on the administration of alkalies.

Another explanation of the renal block must be considered which is not dependent primarily upon the renal block, but is associated with the large doses of insulin which patients are given in diabetic coma. Upon an analysis of these 63 cases it appears that the more insulin they received in general the higher the non-protein nitrogen values. Thus Mary M., Case No. 4232, received 300 units on her first day and her non-protein nitrogen values rose daily as follows: 53, 69, 139 mgm. per 100 c.c. I. J., Case No. 4987, received 350 units upon the first day and her non-protein nitrogen rose on successive days also as follows: 41 and 55 (first twenty-four hours), 72, 106, 115 mgm. per 100 c.c.

[1] Warburg, Acta Med. Scandinav., 1924, 61, 301.

[2] Starr and Fitz, Arch. Int. Med., 1924, 33, 97.

Now if we compare the insulin dosage and the non-protein nitrogens in the two series of coma cases it appears that of 17 cases in the two series receiving 200 units of insulin during the first twenty-four hours 14 had a non-protein nitrogen over 40 mgm., on the first or second day, whereas of 19 cases receiving less than 125 units there were but 3 with a value above that level.

If one examines the 3 cases of diabetic coma associated with "acute nephritis" reported by Bowen and Beck,[1] one obtains further evidence pointing in this direction.

Their cases were tabulated as below:

TABLE 6

THE RELATION OF LARGE DOSES OF INSULIN TO LARGE QUANTITIES OF NON-PROTEIN NITROGEN IN THE BLOOD IN COMA

Case.	Insulin units. First day of coma.	Blood. Urea nitrogen, mgm. per 100 c.c. Day.			
		1	2	3	4
I	350	14	80	102	87
II	265	40	70	70	80
III	190+	30	51		

Suggestive evidence is also afforded in a case report of John.[2] His patient received a large quantity of insulin and later on the third day the urea nitrogen rose to 162 mgm. and still later to 255 mgm. per 100 c.c., but before it had reached this maximum the insulin had been greatly decreased, which is obviously out of harmony with insulin being a factor.

In our cases we attributed the return of the urinary secretion simply to the forcing of liquids of all kinds, salt solution, broths, orange juice, water. Bowen employed in addition to the above sodium bicarbonate and magnesium sulphate, and John used Fisher's solution. It would seem to be evident that the liquids were the important factor.

All of these cases recovered. All had normal kidneys before coma and normal kidneys after coma, and recovery was so rapid

[1] Bowen and Beck, Bull. Buffalo General Hospital, 1925, 3, April.

[2] John, Jour. Amer. Med. Assn., 1925, 84, 1400.

and complete one can hardly ascribe the temporary disorder to an acute nephritis. Is it possible that the anuria was a manifestation of extreme insulin edema?

Edema was observed in 3 of these patients, not noted in 2, and recorded absent in 1 case. Very likely it could have been demonstrated in all if the weights of the patients had been taken daily.

Edema is a common occurrence in the use of insulin, and disappears in coma, and the more severe the case of diabetes, the more apt is it to appear. This may be explained in part by the sudden retention of water, 2.5 grams, for each gram of glycogen stored both in the muscles and liver. The retentions may be overdone with the sudden reduction of the larger quantities of sugar in the blood and possibly to a lesser extent of fat.[1]

Blood-pressure.—The systolic pressure could not be read in 2 cases, was below 100 in 3 others, varied between 100 and 120 in 11 more, and between 120 and 160 in the remaining 8 patients. In our former series 21 cases are reported, and of these the blood-pressure was below 100 in 6, between 100 and 120 in 6 more, and between 120 and 154 in the remaining 9 patients. The systolic blood-pressure in coma under present methods of treatment is therefore not so low as often reported, or in fact as we ourselves have thought.

Glandular.—If there is an interrelationship of glands of internal secretion in diabetes one would expect to find evidence of this during such a diabetic crisis as coma. Three cases, Case Nos. 4306, 5176, 4289, did show as a matter of fact thyroid activation near the period of the coma. This appears like a considerable proportion, but it can hardly be considered as such, because we have had about 100 cases of true diabetes associated with thyroid disease, of whom all have been operated upon and yet only 1 has had coma. It is difficult to say which condition antedated the other in this series. The thyroid activation was recognized in all three before the impending acidosis and the cases seen in consultation by Dr. F. H. Lahey. All three recovered from coma more quickly than is usual, and none had insulin shock.

[1] For a discussion of edema after use of insulin, see references in Von Noorden and Isaac: Die Zuckerkrankheit. ed. 8. Berlin, Springer, 1927, S. 535.

Of the 3 cases of hyperthyroidism with coma 2 were fatal. Case No. 5176 in this series recovered from both coma and thyroid storm to die seven days after the coma from multiple pulmonary emboli and empyema. Patients with diabetes and thyroid disease change their status with surprising rapidity. The ordinary diabetic goes to bed at night mild and wakes up in the morning severe for want of insulin, but the thyroid diabetic's metamorphosis is far more rapid. He almost changes his status like a flash and one must be on the *qui vive* for acidosis, hypoglycemia, and hyperthyroidism. This patient went through all of these states with a suddenness which was surprising to nurses and doctors who have been in close contact with both thyroid cases and diabetic cases for years. A good many punctures of the veins were made and we cannot help thinking that some one of these may have led to the emboli in the lungs which later appeared to lead to a general pulmonary infection, empyema, and death. Possibly the emboli arose in the heart. As auricular fibrillation was present, the pulse rate reaching 270, and the blood-pressure taken three times varied between 55 and 132. Since our experience with pulmonary embolism in this case we have curtailed the number of venipunctures in the course of coma and now depend for many of our estimations on the blood-sugar upon micromethods. It would not be surprising if pulmonary embolism should occur more frequently in patients treated with intravenous injections of glucose and sodium bicarbonate than with patients not receiving such injections. It is for this reason that we report this case. We notice that Foster and Bowen and Beck warn against the dangers of intravenous therapy in coma, though without prohibiting it, or, as a matter of fact, mentioning thrombosis.

Leukocytosis.—A leukocytosis is the rule in coma. Leukocyte counts were made in 19 cases of the series and in but 3, Case Nos. 4710, 4740, 5121, were the number of corpuscles 10,000 or below per cm. The 4 cases with severe infections, Case Nos. 2982, paranephric abscess; 3267, pancreatitis; 4525, carbuncle and peritonitis; 5187, carbuncle, showed a range in the white count from 20,550 to 31,450. In 5 cases the stomach upon la-

vage showed blood. Four of these cases were without the history of an infection and the highest count of all, 81,400, was noted in this group. The range of the count in the 5 cases who were without any apparent infection or hemorrhage from the stomach was 15,000–44,100. In the future observations of the temperature should be recorded coincidently with the making of a white blood-count.

Pulmonary.—Aside from causation of the coma and confusion in diagnosis respiratory symptoms were not prominent save for one remarkable instance, Case No. 3739, who had first an exudate simulating diphtheria of the larynx and later edema of the same. This patient twice required intubation and was saved through the prompt co-operation of the Contagious Department of the Boston City Hospital and its Director, Dr. Place, and by Dr. A. A. Hornor. Edema of the lungs with râles and dulness led us to make a tentative diagnosis of pneumonia in 4 cases of the 30. These diagnoses were refuted by *x*-ray. Pneumonia is by no means as frequent as one would be led to believe by reading certificates of death and coma case reports. It was associated with 1 case, Case No. 2988, however, in our former series.

Treatment.—The principle underlying the treatment of these cases is the treatment of the disease diabetes and not the symptom acidosis. No alkalies have been used; no glucose has been given to protect (!?) the insulin and to offset future possible reactions. Carbohydrate has been given by mouth, usually to the amount of 50 grams in twenty-four hours, so soon as the patients could swallow. When the blood-sugar has fallen nearly to normal and vomiting has prevented retention of food, it has been administered as glucose, but in these cases we have thought it necessary to give it intravenously but 6 times.

The coma patient in reality is a patient in shock. Often he has a low blood-pressure, rapid and weak pulse, subnormal temperature, and is flaccid and comatose. All the routine measures therefore which are employed in the treatment of shock from whatever cause should be utilized, because in doing so there will be a far better opportunity for the insulin to act.

There have been 6 deaths, Case No. 3021 in the early days of insulin within three and a half hours of admission to the hospital, Case No. 3240 with a dilated stomach, Case No. 3267 of pancreatitis, Case No. 4525 with general peritonitis twelve hours after admission, Case No. 5176 with hyperthyroidism and pulmonary embolism, and the last, Case No. 5784, on the thirteenth day after recovery from acidosis, probably of the remote results of alkalosis, though the reaction of the blood was normal two days before death. Our experience with these 63 cases, and our 15 recoveries from impending coma in the pre-insulin days, encourage us to pursue our present plan of treatment without alkalies or glucose along with the insulin.

Insulin is of course the chief weapon by which coma is fought. The initial dose depends upon the depth of coma, the general appearance of the patient, and the blood-sugar level. The first 4 doses have usually been given at thirty-minute intervals. The amount of the succeeding doses is based on the increase or decrease in hyperpnea, and the rise or fall of the blood-sugar and urinary tests. We confess having treated 1 one year and ten month old child in coma, purely on a symptomatic basis with a single test for blood-sugar and the help of three specimens of urine in two days.

The insulin has been administered subcutaneously in all 63 instances of coma, save for 1 or 2 doses in 2 cases. In these 2 patients the patient was so far *in extremis* and the circulation so feeble that we feared insulin given locally would be too slowly absorbed. We believe that whenever insulin is given intravenously that it is desirable to give it subcutaneously as well. The action by the former method is more transitory and probably less active unit for unit under ordinary conditions. In general insulin in moderate doses of 20 units, more or less, every fifteen, thirty, or sixty minutes seems preferable to double, treble, or quadruple the dose at greater intervals, because it appears to act more powerfully in this manner and one can more readily avoid overdosage.

The quantity of insulin administered on the first day averaged 132 units in the first series of coma cases and 166 in the

second; on the second day to 66 units in the first series and 60 in the second, while upon the third day the units were respectively 56 and 49. A glance at the insulin columns of Tables 1 and 2 will show that the dose was adjusted to the needs of the individual patient and not given by rule of thumb. The 6 fatal cases, combining those in Tables 1 and 2, received 80, 60, 240, 497, 215, and 80 units respectively on the first day; the 2 who lived into the second day 175 and 25 units, and on the third day 95 and 25 units. As these 2 cases died at a considerable interval after entrance their dosage is not of significance.

The danger of the alkali treatment of diabetic coma is now supported by clinical evidence in the *occurrence of alkalosis following recovery from coma in one of our patients to whom no alkalies were given.* If our patient without receiving alkalies develops alkalosis, how many there must be who after taking alkalies develop it. This case substantiates our belief in the uselessness and the danger of the alkaline treatment of diabetic coma. Mrs. C., Case No. 5784, with onset of diabetes at the age of fifty-four years, two months previously, was admitted to the New England Deaconess Hospital January 14th, in diabetic coma brought on by fasting and a badly abscessed tooth. She received routine coma treatment. Insulin 80 units in twenty-four hours; gastric lavage; enema; no salt solution. She took carbohydrate 54 grams by mouth. The following day she was out of coma and the abscessed tooth was extracted. During the ensuing week the daily diet ranged as follows: Carbohydrate 60 to 83 grams; protein 34 to 48 grams; fat 47 to 84 grams. On the eighth day after coma she became disorientated. Two days later she had typical tetanoid convulsions with carpopedal spasm. Examination of her blood showed blood-sugar 0.18 per cent., CO_2 80 volumes per cent., calcium 9.6 mgm., and the next day 9.2 mgm. She was immediately given salt solution subcutaneously. The CO_2 fell to 67 volumes per cent. and remained between 43 and 55 per cent. at subsequent observations. The blood-sugar never fell below 0.18 per cent., or rose above 0.48 per cent. The following day she was comatose. She was again given salt solution. On January 27th, from 7.45 A. M. to 8.55

P. M. she had convulsions every few minutes which were general in character. The fundi, ears, spinal fluid, and blood-culture were negative. White blood-count, 15,000. She was afebrile until moribund, when her temperature rose to 105° F. The autopsy revealed no abnormalities to account for death save multiple, scattered, fine punctate, cerebral hemorrhages.

This patient without alkalies developed alkalosis. The insulin which she received, plus her own supply of insulin, set free an excess of basic elements and alkalosis resulted.

Blum was one of the first to describe convulsions[1] after the use of alkalies during treatment of diabetic coma. We are sure it occurs far more often than is reported and we know that this is not always due to failure to recognize it. We advise doctors to leave alkalies alone in diabetic coma.

Fluids are given to replace the extreme loss caused by excretion of the large amounts of urine and the increased ventilation. The need for fluids was especially exemplified by the case of Mary T., Case No. 3739, already cited, who developed an acute laryngeal obstruction during the course of coma treatment. She was given diphtheritic antitoxin during the night as a precautionary measure. The laryngeal obstruction proved not to be due to diphtheria, but to be a dry membranous laryngeal exudate caused by pneumococcus infection and dehydration. The subpectoral administration of saline is preferred to the intravenous, because of the danger of thrombosis, because absorption is more gradual, and because it is far simpler with these patients whose blood-pressures are low.

Peters et al[2] state that "if chlorid can aid in maintenance of the blood reaction by yielding base for neutralization of ketone acids . . . . . the administration of sodium chlorid would seem to be a rational procedure."

Foster[3] has reported 2 deaths during intravenous injection of saline and points out the vulnerability of the heart in cases of coma. He also recommends the intraperitoneal method.

[1] See also Harrop, Johns Hopkins Hosp. Bull., 1919, 30, 63.
[2] Peters, Bulger, Eiseman, and Lee, Jour. Clin. Invest., 1925, 2, 193.
[3] Foster, Jour. Amer. Med. Assoc., 1925, 84, 719.

Lavage of the stomach is now done in every diabetic admission when the CO_2 is below 20 volumes per cent., even without the history of nausea and vomiting. Case No. 3877, despite heroic doses of insulin, was becoming more and more comatose. There was no history of nausea and vomiting. Almost during the lavage which produced evidence of a dilated and full stomach the patient showed clinical improvement. We take no chances with a dilated stomach or even a stomach partially filled with food. Gastric hemorrhage is comparable with the blood found in the feces of dogs in diabetic coma according to F. M. Allen.[1]

An enema is still routine.

Caffein sodium benzoate is given in doses of 5 to $7\frac{1}{2}$ grains every few hours, but we have not given over 35 grains in twenty-four hours, and usually have given less.

Closer clinical observations and micro-blood-sugars are replacing frequent venous blood-sugar and CO_2 determinations. Frequent venipuncture is not without an element of danger as shown by Case No. 5176. It does no harm even if we do exaggerate the danger. We have had so few deaths in coma that we do not wish to take a chance of doing any harm to any patient. A micro-blood-sugar test in coma, performed with capillary blood, may be more useful than a macro-test performed with venous blood. As in our former series, the clinical picture may show vast improvement, while the laboratory still shows the patient to be in deep coma.

The Differential Diagnosis of Diabetic Coma; Coma Due to Hypoglycemia, and Coma Caused by Renal Block with Retention of Non-protein Nitrogen.—It is sometimes difficult to determine which of three types of coma is responsible for the chief symptoms of a diabetic during or immediately subsequent to an attack of diabetic coma. Confusion did occur from misinterpretation of laboratory findings in the case of I. J., Case No. 4978. Fourteen hours after admission, when her condition seemed to warrant it, we ceased frequent tests of the blood-sugar and gave orders for insulin based upon reports of specimens of urine alone. In the following seventeen hours the urine contained

[1] Allen, Jour. Met. Res., 1923, 4, 215.

but a slight trace of sugar and was acid free, yet in spite of this the patient was again unconscious with breathing of the Kussmaul type, and she presented the typical picture of acidosis. This diagnosis was also confirmed by the blood CO_2 combining power which was 14 volumes per cent. The output of urine was scanty, and it was due to its suppression that we had been led astray in our orders for insulin. Although the urine was practically sugar and acid free, it was not representative of the true state as shown by the condition of her blood. When she was given a large dose of insulin she became conscious after a lapse of two hours, but twelve hours later, at midnight, she presented another picture quite new to us. For the third time in the course of two days she was again unconscious. Upon this occasion the respiration was shallow and quite unlike that of diabetic acidosis. The skin was dry and hot, not moist as in an insulin reaction. Her pulse was full and bounding, she was combative, quite the opposite of the usual flaccidity of insulin shock, though occasionally we have known patients in that to be combative too. The blood-sugar by the micro-test was 0.08 per cent. Although this was a nearly normal value we thought the probable cause of her coma was a rapidly falling blood-sugar. Consequently, she was treated for hypoglycemia, but she failed to improve with increased carbohydrate intake. By the following day, September 14th, the riddle was solved for the patient showed the earmarks of nitrogen retention, such as a rising blood-pressure, from 120 on September 12th to 150, non-protein nitrogen of 106 mgm., a large trace of albumin in the urine, a diminished urinary output in spite of an intake of between 2000 and 3000 c.c. of fluid per twenty-four hours.

The cause of the nitrogen retention, presumably brought about by renal blocking, is still unknown. Prior to insulin this occurred not infrequently and we attributed it to the excessive quantity of acid amounting in 1 case, Case No. 4, to 437 grams of hydroxybutyric acid which passed through the kidneys in three days. In those days unless large quantities of urine were voided the patients died after a few hours of coma. With the use of insulin no such amounts of acid are excreted, and yet the

TABLE 7

THE COMA OF DIABETES. THE COMA OF HYPOGLYCEMIA. THE COMA OF NITROGEN RETENTION IN THE SAME PATIENT IN THE COURSE OF THREE DAYS. CASE NO 4978. AGE AT ONSET, 15.9 YEARS. AGE AT COMA, 18.1 YEARS.

Year 1926 Mo. 5 Day 12	Vol. c.c.	Sp. Gr.	Reac	Alb			Nitrogen G	Diacetic Acid	Urine Sugar Reduction %	Urine Sugar Total G.	Diet in Grams Carbohydrate	Protein	Fat	Calories	Naked Weight Lbs.	Non Protein Nitrogen	Blood's Blood Fat %	Blood Sugar %	Blood CO_2 Vol. %	Alveolar air CO_2 mm Hg	Insulin Units Order	Insulin Units Given	Insulin Time Given	Cause of Coma
Hour																								Symptoms
6 A.M.								+++	2.0							41		0.49	9			20		Diabetic Coma). Kussmaul.
7									++++													40		Blood Pressure 130/Resp.
8																		0.43	9			40		
9																						50		
10																		0.33						Conscious
1 NOON																		0.35	13					
2								0	++													10		
3								0	+									0.30	11					
4																						15		
7																		0.23	14			20		
8																						20		
9								0	+							55		0.14	17					
7 A.M.	350							0	+	6	24	6	6	274				0.19	16					
9																		0.30						
1 P.M.																72		0.43	16			40		Diabetic Coma). Kussmaul.
5																		0.40	14			15		Conscious Resp.
10																						25		B.P. 150
12 MID NIGHT	350				0	0		0	0.5	2	42	2	7	239				0.08	21			10		Hypoglycemic Coma).
1½-15	350							0	0	0	42	4	19	355				0.22						B.P. 150
"																106		0.24	26			10		Nitrogen Retention Coma).
15-16	1050							0	0	10	61	13	25	521				0.32				50		
"																115		0.44	25					
16-17	1900							0	0	8	66	26	38	710				0.39				20		
17-18	2250							0	0.5	11	63	41	66	1010							1	40		
18-19	1500							0	1.3	20	64	48	91	1267		90		0.39				40		
19-20	1500							0	1.1	17	60	61	99	1375		60		0.34	39			50		Blood Nacl 0.523 Pr. 11
20-23	750							0	1.0	8	60	61	103	1411										

same condition occurs. At the beginning of her coma she did not show the usual extensive renal involvement in diabetic coma so frequently manifested by showers of granular casts. As soon as this condition of deficient elimination was recognized fluids

CONCOMITANT COMA IN DIABETES

	Acidosis.	*Hypoglycemia.*	*Nitrogen retention.*
Type of onset:	Slow.	Rapid.	Slow.
	Days or hours.	Minutes.	Hours.
Symptoms:	Indigestion.	Hunger.	Headache.
	Nausea.	Weakness.	Nausea.
	Vomiting.	Tingling.	Vomiting.
	Pain.	Trembling.	Labored breathing.
		Sweating.	
	Dim vision.	Double vision.	
	Kussmaul breathing.		
History:	Diet increased.	Diet decreased.	
	Insulin omitted or decreased.	Insulin increased.	
	Infection or hyperthyroidism.	Exercise increased.	
Clinical signs:	Pulse rapid, 130, regular and full at first, later feeble.	Pulse rate normal or slow, irregular.	Pulse, full, bounding.
	Skin dry.	Skin moist.	Skin dry.
	Kussmaul breathing.	Breathing shallow.	Breathing deep.
	Eyeballs soft.	Eyes divergent.	Lucid intervals.
		Pupils dilated.	Combative.
		Drooling.	
	Coma incomplete at onset, but progressive in type.	Coma profound from onset (occasionally combative).	Irregular convulsions.
	Acetone odor.		
	Flaccidity.		
	Reflexes N or absent.	Convulsions.	
Laboratory data:	Blood-sugar over 0.35.	Blood-sugar below 0.06.	Blood-sugar normal or above.
Blood:	Blood CO_2 below 20 volumes per cent.	CO_2 normal or high.	N. P. N. high CO_2 normal, occasionally low.

	Acidosis.	*Hypoglycemia.*	*Nitrogen retention.*
Urine:	Sugar present.	Usually sugar free (second of two specimens sugar free).	Sugar little or none. Volume scant. Albumin present.
	Acetone +.	Acetone.	Acetone 0.
	Diacetic acid +.	Diacetic acid 0. Blood calcium occasionally below 8 mgm.	Diacetic 0.
	Casts in showers.	Casts few or none.	Casts abundant.
Treatment:	Insulin causes slow, progressive improvement.	Insulin makes worse.	Gradual improvement with increased secretion of urine.
		Glucose causes prompt improvement, which may be temporary.	

were increased, subcutaneously as salt solution and intravenously as well, despite her previous supply which we had supposed liberal. The patient improved both clinically and by the laboratory tests in proportion to her increasing urinary output. Her subsequent course was uneventful.

The difficulties which have arisen in this and other cases have led us to tabulate certain features which may be of use in the differential diagnosis in these three types of coma in diabetes. Needless to say other types of coma must always be considered such as that due to apoplexy, drugs, bodily injuries, and as just described—alkalosis. Likewise in any case of coma one must always be on the watch for concomitant conditions which may have induced coma such as infections, either general or local, and of the latter variety particularly those which occur in the abdomen, especially appendicitis.

CLINIC OF DR. HENRY JACKSON, JR.

BOSTON CITY HOSPITAL

THE PROGNOSIS OF CHRONIC NEPHRITIS

OF the three branches of our art, diagnosis, treatment and prognosis, certainly not the least important is the last. The patient may and generally does ask you what is the matter, but he is equally concerned with the problem of how soon he will be well, and consciously or unconsciously his anxiety issues mainly from his concern for the future. Yet in school we hear but little of the difficult art of prognostication. We know in general that the mortality of pneumonia is about 25 per cent. We are taught that tuberculous meningitis is almost—if not quite—invariably fatal. But we are taught largely on a statistical basis—a very proper but a very treacherous foundation for dealing with the individual case. That 25 per cent. of all cases of pneumonia die does not really help us except in a very general way in an individual case. If our 1 case were a true sample of the series on which our general statistical knowledge is based, then his chances of dying would, indeed, be one in four. But the 1 case is never a true sample. If we said of 1000 cases of pneumonia in the hospital 250 will die, our prediction would be near the truth. But on the statistical evidence at hand we could not pick *which* 250 would die; nor could we truthfully say of any individual case his chances of living are three out of four, because they may not be. The prognosis of a boy of fourteen in good general condition suffering from a type one pneumonia is very different from that of a middle-aged, fat, alcoholic man with a type three pneumonia and auricular fibrillation. We need besides a knowledge of the general averages an understanding of the special factors which may influence the outcome—in pneu-

monia, for instance, the type, the degree of involvement, the age of the patient, the condition of the heart, the amount of albumin in the urine, the height of the blood-pressure and the white count. Without these subsidiary factors we cannot prognosticate correctly, for it is these very factors that determine the variation from the statistical mean. What of the outcome of chronic nephritis, a common disease both in hospital and private practice? We have several cases to present today which illustrate some of the points which may help us to decide in this condition the questions so often asked—when shall I be well?—how sick am I?—how long will I live?

Case I.—Mr. C., a single man of forty-two years, entered the hospital two months ago from the out-patient department where he was being treated—quite properly—for painful arthritis of the left hip-joint. It had been found that the urine was grossly bloody and contained a large trace of albumin. He was therefore sent into the hospital for study.

At the time of admission his only complaint was of his hip-joint, which was extremely painful on motion. As a youth he had both syphilis and gonorrhea, but they were treated well and seemingly left no residual effects behind. For the past twenty years he had had attacks of "rheumatism," chiefly in his left hip and both ankles. He gave no history of scarlet fever, tonsillitis, or other infectious diseases except as mentioned above. He was not alcoholic. There were no symptoms referable to the pulmonary or gastro-intestinal systems. Aside from the gonococcus infection years ago there were no symptoms from the genito-urinary tract.

In his mind the present illness concerned itself entirely with the hip-joint, though he had noticed that both ankles were slightly swollen. He had no headache, no eye symptoms, no nocturia. Yet his urine was loaded with pus, blood, and casts. He looked sick.

Physical examination showed, aside from a stiff and very painful hip-joint which does not concern us here, pitting edema of both ankles and a fairly marked pallor of the mucous mem-

branes. The arteries were normal. The blood-pressure was 160/90. The eye grounds—and this is important—were completely normal—no arteriosclerosis, no exudate, no hemorrhages, no blurring of the disks. Otherwise the physical examination was negative.

The red blood-count was 2,500,000 with a low color index. The phenolsulphonephthalein test was 7 per cent. in two hours and ten minutes. The whole blood non-protein nitrogen was 82 mgm. per cent.—a very considerable elevation over the normal value of 30–40. The urine specific gravity was fixed at about 1010, not varying during the "two-hour test" more than three points from that figure. There was about 0.1 per cent. albumin, many granular and cellular casts, and a large amount of blood in the urine—sufficient, indeed, to render the whole specimen red.

The diagnosis is obviously enough nephritis, probably an acute exacerbation of a chronic process. Pure acute nephritis in a man of his age, especially without definite antecedent infection, is notably rare.

What can we say of his future? What prognostic signs and symptoms are there on which we may rely? We must take into account:

1. The eye grounds.
2. The anemia, if apparently due to the nephritis and not to other obvious causes.
3. The blood non-protein nitrogen or blood urea.
4. The 'phthalein output.
5. The general condition of the patient and the presence or absence of associate lesions in other systems.
6. His nitrogen balance.

Albuminuric retinitis associated with chronic nephritis almost invariably carries with it a very poor prognosis. Few cases live over a year or so, though there are exceptions here as in most generalities. A marked anemia is of grave import. Persistently elevated non-protein nitrogen in spite of reasonable dietary treatment generally spells death in a matter of months. The 'phthalein may be low, very low, and yet the patient continue for a long time without obvious ill health, but a gradually

falling 'phthalein test in absence of cardiac involvement is a dangerous sign. Finally we must remember the associated pathology. Has the patient cardiac disease or arteriosclerosis? What is the condition of the other essential systems; their degree of health or disease is most important in predicting the outcome. And finally do not forget that acute infections may completely upset one's hopes and bring about a premature end.

In the case under consideration we gave a good immediate prognosis, largely on the basis of his general good health and the lack of any eye-ground changes in spite of the obviously rather severe flare-up. The low 'phthalein and elevated non-protein nitrogen do certainly mean severe damage, but we are dealing here with an acute flare-up, as indicated by the bloody urine, and we must not lay too great stress on these findings until we see what happens to them during proper treatment in bed. Careful dietary régime and rest in bed was, as a matter of fact, followed by a reduction in blood-pressure to 120/90; the 'phthalein rose to 48 per cent., the non-protein nitrogen fell to 36 mgm. per cent., the red count rose to 4,200,000, and the urine gradually cleared over a period of two months, so that now he has but the faintest possible trace of albumin and an occasional hyaline cast. The urine specific gravity is still fixed; he still has chronic nephritis, but the prognosis, as far as the relatively near future is concerned, is good. One cannot make long-distance forecasts in this disease. The acute flare-up is over. No doubt the kidneys were further damaged during this process, but at present we have no indication that the immediate prognosis is bad. Only careful watching will tell what the ultimate outcome will be.

Case II.—Mr. K., thirty-four years old, entered the hospital the same day as the previous case, with a complaint of epigastric pain and vomiting. He had a markedly alcoholic history and his gastric condition was apparently due to a rather extensive indulgence in prohibition liquor. He further had noticed a persistent nocturia for two months. For the past month he had had severe headaches and some blurring of vision, symptoms not attributable in his case to alcoholism. On entrance he showed

a blood-pressure of 215/160. This persisted until his heart failed, when it fell as it often does in these cases. The peripheral vessels were markedly sclerotic, the heart slightly enlarged to the left. He had no anemia. The urine showed a large trace of albumin, no cells, and a rare granular cast. The eye grounds showed marked albuminuric retinitis, hemorrhages, cotton wool exudate, arteriosclerosis, and blurring of the optic disks. His 'phthalein output was 30 per cent. in two hours and ten minutes. The blood non-protein nitrogen was 34 mgm. per cent., and the specific gravity of the urine was moderately fixed at a low level. He was given a poor prognosis mainly on account of his eye ground changes and in spite of the normal non protein-nitrogen and but slightly reduced 'phthalein. As the days went by his blood non-protein nitrogen gradually rose (although he was on a low protein diet) to 100 mgm. per cent., and the 'phthalein simultaneously fell to zero. His heart failed and he began to have generalized convulsions such as are seen in true uremia. For days he remained in a semiconscious state with occasional short convulsions. The end came suddenly and rather unexpectedly (after a period of apparent improvement) from cerebral hemorrhage—an outcome hinted at by the very high blood-pressure and the marked arteriosclerosis of the smaller vessels seen in the eye grounds.

How did this case differ from the first? Mainly in that his eye grounds showed marked albuminuric retinitis. That his 'phthalein was good and his non-protein nitrogen normal on entrance proved to be of little importance in view of the fact that these signs grew progressively more ominous in spite of all we could do. One cannot prognosticate in this disease from cross-sections. It is a rising or falling non-protein nitrogen, a rising or a falling 'phthalein, an increasing or a decreasing ability to concentrate in the urine that tell the story. No single chemical test gives the key to the situation. A patient with an acute exacerbation of a chronic process, as in the first case, may at first sight appear to be in immediate danger, and yet ultimately recover completely. It is the course, even over a short time, that gives us an insight into the future.

Case III.—Mr. F., thirty-two, entered the hospital in March, 1926, with a history of headache and sudden blurring of vision. A week before entrance he had a severe headache which has persisted to date. A few days after the headache began his vision became blurred, especially in the left eye, and this inability to see became progressively worse. He had had no other symptoms of importance. His past history was negative except for gonorrhea five years ago. The physical examination was quite negative, except for a blood-pressure of 160/100 and very slight changes in both fundi, which were interpreted as possible albuminuric retinitis. The urine contained a large trace of albumin, many red cells, and hyaline and granular casts. In the absence of history of ingestion of toxic agents or excessive tobacco smoking the sudden amaurosis seemed almost certainly due to nephritis, especially in the presence of the urinary findings and the elevated blood-pressure. The eye ground changes were not typical of albuminuric retinitis, but were suggestive.

The blindness cleared rapidly, however, and the urine albumin fell to a very small amount. The improvement was so marked that the condition was thought to be an acute nephritis, and a good prognosis was given. He was followed closely, however, and it was noted that the urine continued to have a slight trace of albumin and a few red cells, and the objective signs in the eyes did not improve. Fresh small hemorrhages appeared and small particles of cotton wool exudate made their appearance for the first time. He disappeared from view and appeared again in the hospital five months later complaining of headache, nausea, and vomiting. The physical examination at that time showed slight puffiness to the face, definite pallor, and well-marked albuminuric retinitis. The blood-pressure, 140/90 on discharge five months before, was now 250/180. The non-protein nitrogen had risen to 54 mgm per cent. on the second entrance, though he claimed to have lived on a low protein diet during the past few months. The 'phthalein, previously normal, had fallen to 25 per cent. The urine again showed a large trace of albumin, many red blood-cells, and casts of all sorts. On account of his marked headache 500 c.c. of blood were

removed with marked improvement of the headache and nausea, and a fall of blood-pressure to 185/145. But the improvement as usual was but temporary and in spite of a very low protein diet (only 10 grams) his non-protein nitrogen rose steadily to 95 mgm. per cent., the headaches returned, the 'phthalein fell to 10 per cent., and he gradually became stuporous. His clinical condition became progressively worse, and he died in coma eight weeks after his second entrance.

Once more the eye grounds should have given us the prognosis. One may see albuminuric retinitis in acute nephritis with subsequent recovery, but these eye grounds got progressively worse in spite of the subsidence of the other signs, and this rapid progress after a temporary clearing gave or should have given a very bad immediate prognosis.

Case IV.—H. F., twenty-five years of age, entered the hospital February 3, 1926, for observation. In 1914 the patient noticed that his urine was red and a few days later his family noticed some puffiness of the face. In the hospital at that time he was found to have a much enlarged heart with a marked systolic murmur at the apex, a blood-pressure of 170/120, a 'phthalein of 30 per cent., and his urine contained large amounts of albumin and many casts. The eye grounds were normal. The non-protein nitrogen was not recorded. During his brief stay in the hospital his blood-pressure gradually fell to 140/80, and the red cells disappeared from his urine, but he still showed a slight trace of albumin and a few hyaline casts. He was followed for several years at another hospital. During these years his 'phthalein remained good, from 50 to 75 per cent., his blood-nitrogen and two-hour test were normal, though he showed a constant trace of albumin and a few hyaline and granular casts.

At the present entrance the blood-pressure was 120/78, the heart was but slightly enlarged to the left. He was putting out about one gram of albumin a day, and the urine contained numerous granular and hyaline casts and a rare red blood-cell. He had no anemia and the eye grounds were normal. In short

a rather long, mild history without functional changes of note and no clinical signs of deterioration.

The prognosis seems good. There are no signs or symptoms of serious import in spite of the rather stormy onset of the process eleven years ago. The eventual outcome is, of course, quite uncertain, but we certainly can say today that with no rise in blood-pressure, no eye ground changes, no anemia, and no elevation of non-protein nitrogen or interference with excretion of dyes the immediate prognosis is excellent.

One last case I should like to speak of because of its importance in private practice. I was called to a nearby town to see a middle-aged man who was known to have hypertension and suspected of having chronic nephritis. On the morning on which I saw him he had been seized with generalized convulsions after a short period of "queer feelings in his head." I found him unconscious with Cheyne-Stokes respiration, and having one generalized convulsion after another. His family physician had given a very bad immediate prognosis. His blood-pressure was 200/100. His eye grounds seemed normal, though, of course, the examination was somewhat unsatisfactory. There was moderate arteriosclerosis of the peripheral vessels. After a venesection of 500 c.c. he recovered consciousness, talked rationally, and after a while went into a quiet sleep. A blood non-protein nitrogen done very soon after venesection showed a normal value. To distinguish true uremia from convulsions associated with cerebral arteriosclerosis may be at the time impossible; absence of elevation of the non-protein nitrogen is strong evidence against true uremia, and a correspondingly better prognosis may be given provided the heart is in good shape and there does not seem to be evidence of a large and increasing cerebral hemorrhage. A good immediate prognosis was given in this case because it was felt that his condition was not uremia. He was seen later at the hospital and all evidence went to show that he had very little nephritis and very considerable cerebral arteriosclerosis. A quiet life, free from emotional and physical strain, should be followed. The eventual outcome depends on many factors.

The immediate outlook is good. A year later he reported as "feeling fine"; he had had no recurrence of his symptoms.

In general what may be said of prognosis in chronic nephritis?

Albuminuric retinitis in association with chronic nephritis spells death in the near future; in association with "pure hypertension" it renders the prognosis uncertain at least. It should be looked for in every case with the pupil well dilated and its progress should be carefully watched.

A steadily rising non-protein nitrogen or falling 'phthalein in the face of rational treatment and rest in bed are of great prognostic importance. The blood chemistry at any one time is relatively unimportant. Witness Cases I and II. It is the progress, the changes, the trend of the findings over a period of time that count. But if the clinical and chemical data do not tally, discard the chemical. Inability to excrete more than 4 grams of nitrogen is of very serious import. Such patients cannot live more than a few months as a rule.

Marked anemia is of serious import. The height of the blood-pressure probably is of little importance except that we are more liable to see cerebral hemorrhage when the pressure is very high. The amount of albumin in the urine is of no importance whatever as far as prognosis is concerned. Cases may die with but a very slight trace and live for years putting out relatively large amounts.

The broad "renal failure casts" of Addis may be of some import—we have no personal experience there. In other respects the type of cast found indicates more the present state than the future outcome.

Finally you should remember that we are trying to evaluate the prognosis of the patient as a whole and not of his kidneys in particular. To be sure, if the kidneys fail completely there is to an end. But remember that whatever objections there may be to the term "cardiovascular renal disease" it remains true that the three systems may be and often are simultaneously involved and that to different degrees. Remember that the renal condition, though perhaps attracting more attention at first, may remain stationary, while the cardiac or arterial changes progress

rapidly to an end; now one feature, now another may gain the upper hand, so that in evaluating the situation in any given case due attention must be given to the patient as a whole.

Finally remember that one may have chronic nephritis for many years, even with reduced function, and yet lead a normal life, and that the prognosis of acute nephritis is quite a different matter from that of chronic.

CLINIC OF DR. MAURICE FREMONT-SMITH

BOSTON CITY HOSPITAL

ON CERTAIN DIAGNOSTIC DIFFICULTIES IN PRIVATE PRACTICE

PRIVATE practice offers one important contrast to the medicine of the hospital ward. Where a pathologic lesion may be shown to exist in a majority of hospital admissions, in private one patient after another is encountered whose symptoms prove to be entirely independent of organic disease. This large group of "maladjusted" is important, first because recognition and adequate (often simple) treatment so often result in improvement or cure; and further, because in individual cases it is by no means an easy matter to decide whether symptoms represent the expression of a basic maladjustment to life, or indicate, on the other hand, the very early evidence of actual disease.

F. McA., a girl of twenty-six, was seen on May 8, 1925, complaining of weakness following a recent attack of fever. She said she had a very slight cough. Her appetite, sleep, and catamenia were normal. Six months previously, following the death of her father, she had had a nervous breakdown, became very depressed, had a "pain in her heart," could not eat, "could not breathe," vomited a great deal, and stopped work. During this episode she had lost 7 pounds, which loss she had not regained.

She was a thin, pale, discouraged, nervous-looking girl. Her mouth temperature was 100.4° F., pulse 100, weight 115 pounds. The pupils, reflexes, heart, lungs, and abdomen were normal. There was slight tremor of the fingers. The urine was negative; blood-pressure, 110 systolic, 70 diastolic. When seen three days later, her temperature was 100.8° F.

This case presents a problem in diagnosis by no means rare. A tired-out, nervous young woman, with a history pointing to an emotional, as contrasted with an intellectual, reaction to the difficulties of life, presents a slight cough and a negative chest.

She has a slight rise in temperature, a rapid pulse and tremor. Are we dealing with early tuberculosis, with hyperthyroidism, or with a tired nervous girl?

An *x*-ray of the chest was reported as follows:

> The chest shows fibrosis and fanlike processes leading from the hyli of the lungs into the first interspaces, but not involving the apices; they spread out rather close to the periphery and we believe it is suggestive but not positive of tuberculosis. The left chest shows more change than the right. There is some peribronchial thickening toward the bases; we believe this area in the first and second interspace on the left to be suspicious.

What does this *x*-ray add to our knowledge of the case?

Fales[1] states that "peribronchial infiltration as seen by Roentgen ray is of no importance in diagnosing pulmonary tuberculosis, as it was not found in any case in combination with positive sputum." However, if we assume peribronchial infiltration to be evidence of lymphatic (early) tuberculosis only, the very pathology would preclude the expectoration of tubercle bacilli. Brown[2] describes the earliest *x*-ray changes occurring in tuberculosis as "more or less thickening and beading along the trunks in a localized area." Heise and Sampson[3] say "we have been frequently impressed with the fact that it is possible for a patient to have clinical evidence of pulmonary tuberculosis without the *x*-ray plate showing any gross densities. However, upon examination, one could see tubercles linearly distributed, concomitant with the pulmonary ramifications which later were somewhat accentuated and at times hazy in appearance."

The *x*-ray in this patient fails to show any parenchymal involvement. There was, however, thickening of the finer bronchioles extending in a localized area in the upper left chest well out into the outer half of the lung. There was also some general peribronchial thickening and the picture, except for the localized area, would be consistent with that seen in chronic bronchitis. By those who ascribe no significance to localized peribronchial thickening the plates would be pronounced negative.

On May 22d a doubtful râle was heard in the region of the third rib anteriorly on the right; on June 3d the chest was negative. The patient's temperature, taken night and morning for a week, did not rise above 99° F. She still complained of a dull pain through the right side.

In September, 1925 she reported that she had been feeling well, though working (except for a few weeks' vacation) all summer. She had had no pain, cough or vomiting. Her weight was 122 pounds, pulse 72, temperature 98.4° F.

At this point it would be difficult and probably unwise to make a diagnosis of tuberculosis; certainly the gain in weight, slow pulse, and normal temperature are not consistent with an active process, and the fact that her improvement did not coincide with any environmental change suggests that her previous upset was probably not due to pulmonary tuberculosis. Much the same reasoning applies to the possibility of hyperthyroidism. Certainly a pulse rate of 72 in the office is not consistent with any present increase in basal metabolism.

Early in November she developed a fever of 103° F., vomiting, cough, and pain in the side. A week later her pulse was 114, temperature 101° F. The right back was flat to the angle of the scapula, with the accompanying signs of fluid. The patient was sent to a sanitarium, whence she was discharged six months later with a gain of 14 pounds and a normal temperature and pulse.

Little question now of the diagnosis. Even the original symptoms take on new significance, and one asks why the diagnosis was ever in doubt. Early in the disease, however, certainty of diagnosis is frequently impossible.

In view of the frequent necessity for differentiating between tuberculosis, hyperthyroidism and neurosis, and the occasional great difficulty in so doing, it is interesting to review the symptomatology of these three conditions as shown on p. 1320.

A few points about pulmonary tuberculosis bear restatement: (1) "Neurasthenic symptoms" occur more frequently in tuberculosis than in any one other disease. (2) In cases in which the symptoms of neurasthenia predominate, physical examination of the chest frequently fails to discover definite evidence of tuberculosis; moreover, *x*-ray may be suggestive only, or in cases limited to the pleura, frankly negative. (3)

Early tuberculosis.	Neurasthenia.	Hyperthyroidism.
Onset insidious.	Onset insidious.	Onset usually insidious.
Loss of strength.	Loss of strength.	Loss of strength.
Loss of endurance.	Loss of endurance.	Loss of endurance.
Loss of appetite, especially for breakfast.	Loss of appetite.	Appetite increased.
Eructations common.	Eructations common.	Eructations common.
Nausea common.	Nausea very common.	Nausea and vomiting present in acute cases.
Vomiting occasional.	Vomiting common.	
Diarrhea may be present.	Diarrhea not uncommon.	Diarrhea not uncommon.
Insomnia occasional.	Insomnia common.	Insomnia common.
Palpitation common.	Palpitation very common.	Palpitation very common.
Nervousness.	Nervousness.	Nervousness.
Skin moist and warm.	Skin moist and cool.	Skin moist and warm.
Amenorrhea not infrequent		Amenorrhea frequent.
Hoarseness persistent.		
Cough persistent, slight.		
Hemoptysis.		
Pleurisy.		
x-Ray usually positive or suspicious.	*x*-Ray negative.	*x*-Ray negative.
Fever usual.	Temperatures 99.5° F. not uncommon.	Slight fever not infrequent.
Pulse rapid.	Pulse rapid, inconstant.	Pulse rapid, constant.
Loss of weight.	Loss of weight common.	Loss of weight.
Tremor not common.	Tremor common.	Fine tremor constant.
Metabolism + if fever.	Metabolism normal.	Metabolism + 20 or over.

Râles which may be absent in the morning may be audible in the afternoon or evening. (4) Diagnosis for or against minimal or incipient tuberculosis can rarely be made at the first examination.

Cough, otherwise unexplained, lasting seven to eight weeks, excites suspicion of tuberculosis. Cough may, however, be so slight in the early stage of tuberculosis that it goes unnoticed by the patient. The small repeated morning hack, characteristic of early pulmonary tuberculosis, is often disregarded by the laity, to whom "cough" means something deeper and more "bronchial." Cough may be present only on arising; rarely it

may be even entirely absent in patients showing physical signs in the lungs and a positive roentgenogram, as some patients free the larynx of hypersecretion not by cough, but by clearing the throat, a symptom often discovered only by direct questioning. The absence of cough, although a strong point against, therefore does not absolutely rule out tuberculosis of the lungs.

Persistent *hoarseness* is always minimized by the patient, and is, on the other hand, always of importance. If not caused by local laryngeal disease (papilloma, carcinoma, or syphilis) or by mediastinal pressure from aneurysm, dilated right auricle or intrathoracic tumor, tuberculosis of the lungs must be suspected. Many cases of pulmonary tuberculosis develop hoarseness as the first and for a time the only definite symptom. In the presence of slight cough or persistent hoarseness what shall we say of the *negative physical examination*. Heise and Sampson[3] studied 235 cases of tuberculosis, of which 19 gave no definite physical signs; 84 per cent. of this group of 19 gave definite *x*-ray evidence of tuberculosis. By contrast 9 per cent. of 68 cases classified by history and physical signs as incipient tuberculosis, failed to show a lesion by *x*-ray. Fales,[1] in a study of 411 cases, found a positive sputum in over half the cases without physical signs, but showing *x*-ray evidence of tuberculosis of the lungs. It can thus be seen that no absolute reliance may be placed on a negative physical examination of the lungs in the elimination of early or latent pulmonary tuberculosis.

Hemoptysis is alone presumptive evidence of tuberculosis if other possibilities such as mitral stenosis or the history of recent influenzal infection be eliminated. Throat conditions may be practically excluded as a cause of real hemoptysis. In cases in which hemoptysis comes out of a clear sky, physical signs, fever, and a positive *x*-ray may all be absent. It must be conceded, moreover, that many of these cases never develop clinical tuberculosis of the lungs. In spite of the negative evidence, however, tuberculosis must be considered as the first possibility.

Pleurisy is frequently the first symptom of pulmonary tuberculosis, and if accompanied by effusion, is alone presumptive

evidence of tuberculous infection. Such infection may be for long periods limited to the pleura, patients giving a history of repeated mild attacks of pleurisy before pulmonary disease is demonstrable. In other cases pleural infection apparently becomes permanently arrested and parenchymal involvement does not follow; but it is significant that of the patients entering a tuberculosis sanitarium with definite lung signs a very large proportion give a history of previous pleurisy. Pleurisy at an apex, a symptom often mistakenly diagnosed "rheumatism," is said to be very suggestive of tuberculosis.

Fever is one of the most difficult of symptoms to interpret. Its very definition and the methods of its determination are both uncertain. It is a common belief that mouth and rectal temperatures differ always by a given definite amount ($\frac{1}{2}$–1°). This belief is erroneous. The mouth and rectal temperatures are sometimes identical, more often at variance, the difference (even when the usual precautions in taking mouth temperatures are observed) in certain instances exceeding 2 degrees.* A mouth temperature of 100° F. may thus represent an actual fever of 101.5° F. or even 102° F., or it may rarely represent a rectal temperature of 100° F. If an accurate knowledge of the body temperature is desired, the temperature must be taken by rectum.

Many apparently healthy people show in the office a mouth temperature of 99.5° F. Any rise above this figure demands explanation. Nervous individuals without disease, after slight exercise or excitement, as normals after more active exertion, may show a mouth temperature of 100° F. The normal rectal temperature in an individual at rest does not exceed 100° F.[4]

The temperature in the tuberculous patient, as in the neurotic, is abnormally labile, slight exercise or excitement causing a definite temporary rise. It is worth noting that some tuberculous patients show an afternoon rather than an evening rise, and estimation of temperature made late in the day may be deceptively normal. On the other hand, fever may be entirely absent in pulmonary tuberculosis. It is not extremely unusual

* Observations to be reported.

to find an active, progressive case with a constantly subnormal temperature. In such cases the pulse, which is without exception rapid, is the criterion upon which to depend. Slight degrees of fever are not infrequently present in hyperthyroidism; on the other hand, in the presence of fever from any cause, an increased metabolic rate is the rule.

Pulse.—The pulse rate in active tuberculosis is usually increased. Here again the comparison between neurosis, hyperthyroidism, and tuberculosis is interesting. In hyperthyroidism the pulse remains constantly elevated; sleeping or waking, the increase in rate persists. Not so in the neurotic. Here the pulse may reach 120 per minute at the first observation in the office; fifteen minutes later after reassurance it may drop to 75 or 80, and with the patient asleep it may be caught at an even lower figure. The pulse in early tuberculosis follows a middle course. There is usually a constant elevation, even though the patient be comfortable and in bed; slight exertion or excitement, however, markedly raise the rate. It may be high, unaccompanied by fever.

Symptoms of neurasthenia as already stated are more common in tuberculosis than in any one other disease. The same complaints: loss of strength and endurance, loss of appetite, eructations, insomnia, palpitation, and nervousness occur in both neurosis and tuberculosis, and may be so marked in some early cases of the latter that the underlying tuberculous condition is completely masked. Many physicians tacitly ascribe to themselves an instinctive ability to sift the chaff from the wheat, differentiate at a glance the neurotic individual from the tuberculous. One must remember, however, not only that the neurotic is subject to tuberculosis, but that a latent tuberculosis may by itself be responsible for the inability of the individual to make the adjustments compatible with normal life; that tuberculosis may thus be the causative background for a neurosis.

The following case* presents, in a different field, a problem similar to that just discussed:

* This case referred to in an article on the eye, Boston Med. and Surg. Jour., 194, 968, May, 1926.

A. M., an unmarried woman of thirty-five, was seen April 18, 1925, complaining of numbness of both feet and legs, noticed for three weeks. The legs were not weak, there was no difficulty in motion. The night before admission she felt tingling in the fourth and fifth fingers of her right hand, and numbness of the left arm to the elbow. She felt tired, but otherwise had no complaints. Until the day before admission she had been at work as operating-room nurse in a large hospital. She had lost 25 pounds in the last year.

The past history was unimportant until 1916, when an antrum became infected and was drained. In 1920 she developed partial loss of vision in her left eye, and for one week could not count fingers. A diagnosis of retrobulbar neuritis was made by a competent ophthalmologist. Complete vision was regained. One year later she had transient numbness of the right side of the face, lower gums, and tongue. The tonsils were removed and these symptoms disappeared. In 1924 she had pyelitis for a month. Her bowels, which had been regular, became constipated, and this condition persisted.

Persistent numbness of the extremities always suggests the possibility of a lesion in the spinal cord. It is a symptom occurring in tabes, in primary anemia, and in some cases of cord tumor. It may occur also in multiple sclerosis, and may be a manifestation of hysteria.

In primary anemia the cord degeneration may appear at any time during the course of the anemia, or may precede the blood changes by even years. The degeneration is usually diffuse, affecting both posterior and lateral tracts, with a resulting ataxic paraplegia. The reflexes are increased, Babinski is positive and clonus present (lateral pyramidal tract injury), there is loss of superficial sensation, decrease or loss of toe position sense and vibratory sense, and ataxia (posterior tract injury). There is characteristically no definite upper level of sensory disturbance; degeneration may extend to the cervical region and cause similar changes in reflexes and sensation of the hands and arms. Much less frequently the process is limited to the posterior tracts, resulting in a true tabetic picture, with ataxia, absent reflexes, lightning pains, and even girdle sensations (Osler). Such a condition would be differentiated from true tabes by a consideration of pupils, fundi, blood-picture, and spinal fluid.

Cord tumor is classically associated with early root pains; but pain may be entirely absent, and the condition closely

resemble that of a slowly progressive degeneration of the cord. The point of difference is the demonstration in cord tumor of a definite upper level of sensory disturbance, a finding which points to a localized rather than a diffuse pathologic condition. Moreover, in any tumor of sufficient size to give evidence of cord compression (reflex changes and objective sensory disturbance), subarachnoid block can be demonstrated, often by lumbar puncture alone. Absence of the normal rapid rise of fluid in the manometer on correctly performed jugular compression, abnormally rapid decrease in the pressure upon the withdrawal of small amounts of spinal fluid, and a high protein content (quantitative analysis) together with a low cell count, are the characteristic findings of subarachnoid block.

To proceed with the examination of this patient:

She was a well-developed and well-nourished woman of thirty-five, nervous and mentally depressed. She was of good color. Blood-pressure was systolic 110, diastolic 70. The pupils were equal and reacted to light; ocular motions were normal; the fundi were negative. There was no cranial nerve paralysis. The tongue was normal; teeth and throat, glands, breasts, and thyroid negative. Lungs and heart were negative. The right kidney was palpable, abdomen was otherwise negative.

The knee-jerks were equal and moderately active, ankle-jerks equal and normal. Biceps and triceps normal. There was no clonus and no Babinski. Vibratory and toe position sense were normal. There was no ataxia of legs. Romberg was negative. Sensation for pain and touch was normal.

Blood Wassermann was negative. Red count, 4,650,000. White count, 6700. Differential, 83–12–3–2. The red cells were normal in size, shape, and color. Platelets were normal.

Here again are we dealing with a nervous, poorly adjusted individual, with hysterical manifestations, or with a degenerative condition of the central nervous system? In favor of some sort of actual pathologic change were her previous robust health, her transient loss of vision five years before, the temporary anesthesia of the face a year later, and the present numbness and tingling of her extremities. In favor of neurosis or hysteria were the glove-like distribution of her sensory symptoms ("numbness in both feet, less marked in legs up to knees, back and front"), the lack of confirmatory evidence on objective examina-

tion, the entire absence of objective evidence pointing to organic cord or blood disease, and last, her emotional reactions during examination, which were manifestly of the hysterical type. It seemed, moreover, logical that with definite symptoms appearing five years previously, some evidence of organic change should now be discoverable had these early symptoms been due to early actual disease. Arguing along these lines a diagnosis of hysteria was made.

In January, 1926, nine months later, Dr. George Clymer found that her speech was scanning, "she had a slight intention tremor, nystagmus, double Babinski, and suggestive though unsustained ankle clonus. I think there is no doubt at present that the diagnosis is multiple sclerosis."

The patient died December 11, 1926, twenty months after the onset of symptoms. At autopsy scattered patches in the dorsal and lumbar cord were found, firmer than the surrounding tissue, pale, translucent, and irregular in outline. Microscopic examination showed proliferation of the neuroglia, especially in relation to the areas described above, collections of small mononuclears throughout the perivascular spaces, and abundant lymphoid cells throughout the gray and white matter of the cord. Diagnosis, "multiple sclerosis."

Multiple sclerosis is of organic nervous diseases the one most frequently mistaken for neurosis. General paresis may in its early course present nervousness, irritability, and insomnia as sole symptoms, but even at this stage the pupils usually show suggestive abnormality. Multiple sclerosis, on the other hand, may for long periods give no characteristic symptoms or signs.

Multiple sclerosis is a disease of the young, and is more common in females (Osler). The onset is variable as would be expected from the pathology: "isolated or disseminated patches of sclerosis scattered over the entire nervous system." Sometimes a transient ocular palsy or a transient blindness (as here) ushers in the disease. Sometimes weakness of the legs is the first symptom. Sensory disturbances are not prominent, but Sittig[5] has called attention to the frequency with which fugitive, rapidly shifting paresthesias occur in this disease. Emotional instability is a frequent finding, and marked remissions are characteristic.

Of the early signs, absence of the abdominal reflexes and pallor of the temporal sides of the optic disks are the most constant. Later the classical picture appears: Scanning speech, nystagmus, and intention tremor. Other symptoms described are uncontrollable laughter and incontinence or retention of urine.

It is evident that in this case more attention should have been paid to the past history of loss of sight and transient facial anesthesia, as indications of organic disease. Primary anemia was considered and ruled out, but as during physical examination multiple sclerosis was not thought of as a possibility, I find no statement in my notes as to the condition of the abdominal reflexes, or specifically as to nystagmus. A lumbar puncture here might have cleared up the diagnosis or, on the other hand, might have been indeterminate. In many cases of multiple sclerosis the spinal fluid will show an abnormal goldsol curve, and may show 15 to 30 cells and increased protein. In about half the cases, however, the fluid is normal.

It is thus well for the practising physician, so frequently called on to make a diagnosis of functional disease, to review from time to time a few of the various organic conditions which in their early stages may closely mimic the effects of maladjustment. Though the great majority of diagnoses should remain unchanged, the physician's outlook is enlarged, and even the group of "probable neurasthenics" becomes a field of interesting diagnostic speculation.

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CLINIC OF DR. LEWIS WEBB HILL

CHILDREN'S HOSPITAL

GLUCOSE AND INSULIN IN THE TREATMENT OF RECURRENT VOMITING

T. P., aged five years, was first seen by me in consultation September 4, 1922.

Family History.—Not remarkable.

Past History.—In the last year he has had two vomiting attacks similar to the present one. His tonsils and adenoids were partially removed three years ago. He has always been a somewhat delicate child, but has had no serious illnesses other than the vomiting attacks.

Present Illness.—He was perfectly well up to September 2d, when he suddenly began to vomit, and had vomited persistently up to the time he was seen. There is no history of indiscretion in diet or other apparent cause for the vomiting. He is extremely thirsty, and cries continually for water, which he immediately vomits. He has had no diarrhea, and his temperature has not been over 100.5° F.

Physical Examination.—He is a very sick boy. The eyes are sunken, and he is very restless. There is marked salivation, and he is continually spitting. The neck is not stiff or tender. The pupils are normal. The tongue is heavily coated, and the breath has the sweetish odor of acetone. There is no hyperpnea. There is considerable tonsil tissue on the right side, which is red and inflamed. The heart and lungs are normal. The abdomen is much sunken, and a few small glands can be felt along the course of the sigmoid. There is no tenderness or spasm.

He was given ice cold orange juice and sugar, 2 teaspoonfuls every ten minutes, and 5 per cent. glucose by rectum, 6 oz. every three hours. The next day he was no better, and was

still vomiting every few minutes, so he was brought from the seashore, where he had been, and was placed in the private ward of the Children's Hospital. His breathing was definitely hyperpneic, and what little urine he passed was loaded with acetone and diacetic acid. He was given 600 c.c. of normal saline subcutaneously and 300 c.c. of 2 per cent. glucose solution intravenously.

He vomited several times in the next twenty-four hours, but gradually began to improve, and by the next afternoon was able to keep down small doses of orange juice and sugar. In the next few days his vomiting ceased, but his abdomen became somewhat distended, and very rigid and tender, especially in the right upper quadrant. This was evidently due to an enlargement of the liver, which could be easily felt three fingers below the costal margin, and was extremely tender. He gradually improved, was discharged in a few days, and was up and around again soon after.

His next attack began on August 9, 1923. This started as suddenly and with as little apparent cause as the first. He was again at the seashore, and had been vomiting for two days before he was brought to Boston. He was given 5 per cent. glucose by rectum and 275 c.c. of 10 per cent. glucose intravenously. His vomiting did not stop at once, but he gradually improved as he did before, and was discharged in about a week. During the height of this attack his blood-sugar was 80 mgm. per 100 c.c. blood, and his plasma bicarbonate was 24 volumes per cent.

In the next six months he had no more attacks, but was much below par generally. Each time he was seen his remaining tonsil tissue looked unhealthy, and it was possible to squeeze a little pus from the remnant of the right. Since his tonsils were definitely diseased, it was decided to clean out the throat, as it was felt that infection in the tonsils was not only pulling down his general health, but might also be a factor in causing his recurrent attacks of vomiting. This was done April 14, 1924. He began to vomit immediately after the operation, and went off into the worst attack he had ever had. He was given 300 c.c.

of 10 per cent. glucose intravenously, which apparently did no good whatever, and his condition soon became precarious. He was markedly hyperpneic, and was in semicoma, with a poor pulse and cold extremities, retching continually, and vomiting bile stained with blood. He was then given 300 c.c. of 10 per cent. glucose solution intravenously, and 10 units of insulin subcutaneously.

He did not vomit once after the glucose and insulin injections; he almost immediately brightened up, and made a quick and uneventful recovery.

In November, 1924 he had another, but apparently milder attack, which stopped without any special treatment. I did not see him during this attack, and the family doctor called in a surgeon, because this time the boy had a good deal of spasm and tenderness in the right lower quadrant. They both felt that the appendix was at fault, and that it might well be the underlying cause of all his attacks, so in December, 1924, the appendix was removed. A good many adhesions were found about its base, but otherwise it was not particularly abnormal. It was fervently hoped that with the tonsils and appendix removed, his vomiting attacks would cease, but such was unfortunately not the case.

He had severe attacks on September 26, 1925, and February 24, 1926, which were immediately stopped by the usual treatment with glucose and insulin. Each time it worked exactly as it did the first time it was given: immediate cessation of vomiting, quick disappearance of the acetone bodies from the urine, and great improvement in his general condition.

We have here, then, a boy subject to severe attacks of recurrent vomiting, usually associated with a real acidosis. Removal of the tonsils and of the appendix apparently did him no good. In three attacks he was given glucose and insulin, which was an absolutely specific treatment for his particular disorder. Glucose alone, without the insulin, was found to be comparatively ineffective.

Discussion.—We are much in the dark as regards the etiology of recurrent vomiting. Although it was first described by

Gruére as long ago as 1849, and although a good deal concerning it is to be found in the literature, it is discouraging to realize that what we actually know is very little. This is partly due to the fact that most cases of recurrent vomiting are treated at home in private practice, and that consequently there has not been the opportunity for careful laboratory investigation that there would be were it more of a "hospital" disease.

The well-ascertained facts are at present too meager upon which to base any adequate theory of etiology, and are about as follows:

1. It is more likely to occur in children with highly strung nervous systems.

2. All the evidence indicates that some profound disturbance of the carbohydrate metabolism occurs during an attack.

3. Prominent as exciting causes are:

   (*a*) Physical or mental overstimulation.

   (*b*) The onset of acute infections (tonsillitis).

   (*c*) Physical abnormalities of the digestive tract, such as adhesions, ptosed stomachs, elongated and sacculated sigmoids (Kerley).

   (*d*) Poor posture (Talbot).

4. The acetonuria often occurs before the vomiting. The vomiting is therefore not the sole cause of the acetonuria, and it is also unlikely that the acetonemia is the sole cause of the vomiting. They are both rather different expressions of a common cause.

5. During an attack the creatin in the urine is increased, as well as unodixized sulphur and uric acid. Lactic acid and indican are present in the urine (Howland).

6. In the only cases (5) reported in the literature where blood-sugar determinations have been made, it was found to be low (Hilliger, Bass and Josephs, Meyer and Bamberg, Knoepfelmacher).

7. If the attack is a severe one, the carbon dioxid combining power of the blood may be low, and a serious acidosis may be present.

8. As far as we know, diet probably has very little to do with the condition.

It must be concluded that for some at present unknown reason certain children, the subjects of "recurrent vomiting," are unable at times to utilize carbohydrate, and burn fat instead, which gives rise to the characteristic acetonuria. In these children, withdrawal of carbohydrate from the diet produces lowering of the blood-sugar more readily than in a child not the subject of recurrent vomiting. From this one would suspect that glycogen storage or glycogen mobilization and oxidation might be deficient. In one case investigated by Wilson, Levine, and Rivkin glycogen storage was found to be normal, and between attacks, during short periods of fasting, the quantity of carbohydrate mobilized and oxidized was not diminished.

From this brief summary it may be seen how woefully few and inadequate our data are as to the metabolism in this condition, and it will never be understood until a great many more facts are accumulated.

Treatment.—This may be divided into two phases: between attacks and during attacks.

1. Inasmuch as it is well known that children who are subject to recurrent vomiting are usually of the highly strung, nervous type, and that nervous or physical exhaustion will often precipitate an attack, it is of great importance to regulate the life of the child in such a way as to avoid excitement and over-exertion. The daily rest should be insisted upon, the play should be carefully controlled, and children's parties and long automobile rides should be avoided. I have seen a good many attacks brought on by these last three.

2. Practically all children with recurrent vomiting are dieted very carefully, and still may continue to have attacks. It is very doubtful whether diet has anything to do with the condition, and yet on theoretical grounds a diet low in fat and rich in carbohydrate would seem indicated. The normal child burns carbohydrate in preference to fat: the recurrent vomiter at the onset of an attack burns fat, either because he cannot for some reason burn carbohydrate, or it is not there for him to

burn. It would seem reasonable to provide a liberal amount of carbohydrate for these children in the diet at all times. This would mean a light lunch of crackers or fruit between meals, and especial care to provide easily absorbable carbohydrate at the onset of any acute infection or during any time of exertion or excitement. From what little we know about the disease, this would seem to be about the only dietary therapy indicated.

3. In not a few cases acute tonsillitis precipitates an attack, and if the child is subject to acute upper respiratory infections, the tonsils and adenoids should be removed. This was especially emphasized by Sedgwick in 1912, who reported 8 cases entirely cured by tonsillectomy. I have myself seen one such case, a child who had such frequent and severe attacks that she was incapacitated most of the time. After tonsillectomy she never had another attack, and gained weight in an extraordinary manner.

4. In certain cases there may be found structural abnormalities of the digestive tract, such as ptosed stomachs or adhesions. Correction of these may help, and it is always worth while in any severe case to have a Roentgen-ray examination of the digestive tract in order to detect any such abnormalities. Recurrent attacks of appendicitis may sometimes be the apparent cause of the vomiting, and C. G. Mixter has reported a series of cases, some of which had all the earmarks of recurrent vomiting, which were either cured or greatly relieved by removal of the appendix. There can be no question that various abnormalities of the digestive tract may be associated with digestive upsets in which vomiting is a prominent symptom. There is some doubt, however, as to whether these cases should be classed as true recurrent vomiting, and it is well to proceed with a good deal of caution before resorting to operation, as in not a few cases it may be of no benefit.

5. *Posture.*—Talbot and Brown in 1920 called attention to the fact that many children with recurrent vomiting have a poor posture, with lordosis, "round shoulders," and protuberant abdomen. They found that correction of the posture, and the use of a small supporting pad to correct the position of the

ptosed abdominal viscera, brought about a cessation of the vomiting attacks in several cases, and they regard poor posture as a very important factor in producing the clinical picture of recurrent vomiting.

Treatment of the Attack.—At the onset the lower bowel should be emptied by enema. There are only two cathartics which are worth while trying, as anything else is sure to be vomited, and to irritate an already irritable stomach. These two are milk of magnesia and calomel. A teaspoonful of milk of magnesia may be given every half hour until 6 teapoonfuls have been taken. Some of this will be vomited, but enough may be retained to do some good. This is probably better than calomel, but if the child rebels against magnesia, as is often the case, a grain of calomel may be given in divided doses.

Food.—A child with recurrent vomiting will vomit anything that is put into his stomach. It is therefore a question whether or not to put anything into his stomach. Some writers have advocated giving nothing whatever by mouth until the attack was over, others believe in giving small amounts of carbohydrate food, whether it is vomited or not. At present I agree with the last group for two reasons. In the first place, thirst is often intense, and it is a great deal easier to keep the child quiet and comfortable if he is given fluid by mouth. In the second place, there is no evidence to show that the vomiting stops more quickly when food is withheld than when it is given, and it is probable that a considerable amount of the carbohydrate given is absorbed and utilized between vomitings. If this happens, it is, of course, of great advantage, as the chief purpose of therapy is to get carbohydrate into the system. Orange juice or pineapple juice with the addition of cane-sugar is the best food to use. It should be given ice cold, frequently, and in small amounts: A tablespoonful every fifteen minutes. When the vomiting stops, a thick cereal gruel, and crackers or toast, may be used. Milk should be returned to very cautiously.

Rectal feeding should be begun as soon as the attack starts, and 4 to 6 ounces of a 5 per cent. glucose solution can be given

in this way every four hours. For most children this is more efficient than the Murphy drip.

It seems not unlikely that the vomiting is a central affair, and is caused by disturbance of the nervous control of the stomach rather than by direct irritation of the stomach itself. Sedatives should therefore be of some value, and this is found to be so in practice. If a child who is vomiting every few minutes, and who is restless and irritable, can be given a night's sleep, he not infrequently awakes with a tolerant stomach. The old combination of chloral and sodium bromid, given by rectum, will often accomplish a great deal. Five grains of chloral and 10 of bromid may be given in this way to a child of five years.

Intravenous Therapy.—Many attacks of recurrent vomiting are not severe enough to need intravenous therapy. In not a few instances, however, the child may become extremely sick, much desiccated, and may show signs of severe acidosis (hyperpnea). Under such conditions, carbohydrate should be given intravenously in the form of 10 per cent. glucose solution, about 300 c.c. to an eight-year-old child. There is no guarantee, however, that the glucose will be burned. In the first place it must be given very slowly, much more slowly than most people ever give it, and in the second place it is quite possible that in the condition we are discussing the power to burn carbohydrate is impaired. What is very likely to happen is that the glucose solution acts as a diuretic, and most of it appears in the urine in a short time.

The use of insulin with the glucose is a rational procedure. Although glucose and insulin must have been used frequently in treating recurrent vomiting, I can find only two reports concerning its use in this condition, both in 1925. Meyer and Bamberg gave 500 c.c. of 12 per cent. glucose intraperitoneally, and 15 units of insulin to a very severe case, which was practically moribund. The vomiting stopped at once, and the child recovered. Greer reports 2 cases to which he gave glucose subcutaneously without any benefit. He then gave 300 c.c. of 5 per cent. glucose subcutaneously with insulin. In both cases

the vomiting stopped within twenty minutes after giving the insulin, the acidosis cleared up at once, and both children rapidly recovered. In the case I have been discussing with you there was opportunity to use the glucose and insulin treatment (1 unit of insulin for each 3 grams of glucose) three times, each time with truly remarkable results. Not only did the boy never vomit after receiving the glucose and insulin, but his whole condition changed at once. His salivation lessened, he became brighter and more interested in his surroundings; in short, he was each time changed at once from a dangerously sick child to a convalescent one. *The treatment for this child is an absolute specific, and an attack can be stopped at any time.*

No final conclusions can be drawn from so few cases, but it may be possible that intravenous or subcutaneous glucose with insulin is as much a specific for the carbohydrate disturbance present in recurrent vomiting, as insulin is for the acidosis of diabetes. The two conditions are in certain respects similar. There is an inability to utilize carbohydrate in both, which brings about the incomplete combustion of fat, and hence acetone body production. In the former there may be either an inadequate supply of reserve carbohydrate (glycogen) in the liver, or else an inability to use it, and on account of the vomiting it cannot be supplied with any certainty by mouth. In the latter there is plenty of carbohydrate available, but an inability to burn it. The end result, incomplete fat combustion, is much the same in both conditions, although in recurrent vomiting there is probably some additional factor present, as it does not seem likely that the acetone body production accounts for the whole picture. In diabetic acidosis the acetone bodies do not ordinarily cause vomiting, and in other diseases their presence is the result of vomiting. In this disease they may appear before the vomiting, and even if they do not directly cause it, they must have a good deal to do with it, for when carbohydrate is burned in the body they quickly disappear, and the vomiting stops.

OVERFEEDING WITH MILK ("MILCHNÄHRSCHADEN" "BILANZSTÖRUNG")

THIS baby is five and a half months old. There is nothing noteworthy about his family history.

Past History.—Full term, forceps delivery. Birth weight 9 pounds. He was breast fed for two months, then was weaned and was put on a rather concentrated mixture of whole milk, water, and dextrimaltose. Since he was four months old he has been taking

Whole milk	36 oz.
Water	12 oz.
Dextrimaltose No. 1	3 level tablespoonfuls

Present Illness.—The chief complaint is that he does not gain weight and has a tendency to eczema. He gained well up to about a month ago, when he weighed 17 pounds 12 ounces, then remained stationery for about two weeks, and in the last two weeks has lost over 2 pounds. He now weighs 15 pounds.

He takes his food well, and has never vomited. His stools for the last few weeks have been very constipated, dry and crumbly, and vary in color from pale yellow to a grayish white. He has never had fever or sickness of any kind. His eczema has varied, but has never been very bad. He has had one or two dry patches on his face, and at times moist eczema back of the ears.

Physical examination shows a large baby in apparently fair nutritional condition. When he is examined more closely his flesh is found to be soft and flabby, and does not have the characteristic firm rubbery feeling which the flesh of a baby in good nutritional condition should have. Physical examination is otherwise not remarkable.

Discussion.—There are two things that strike us in this story:

1. His rather large loss of weight in spite of an apparently adequate caloric intake, without any symptoms of indigestion, or disease of any sort.

2. The unusually light color of the stools, which at times are almost white.

Let us analyze his diet. It is apparent at once that he has for some months been taking a rather large quantity of milk, about 2½ ounces per pound of body weight. It is also apparent that he is taking a relatively small amount of added carbohydrate—about 1 ounce. If we compute the calories of his diet, we find that he is getting 840 calories, or 56 per pound. This certainly is adequate.

It is not enough to look at the food as a whole; we must next consider the ratio of the food elements to each other, and we find that the percentage composition of the food is as follows:

Fat	3.0
Sugar	5.3
Protein	2.5

He is then taking a food relatively high in fat and protein, and relatively low in carbohydrate. Owing to the large quantity of milk, he is also taking a large amount of calcium.

This type of nutritional disturbance was first described by Czerny, who called it "Milchnährschaden" (milk injury), and later by Finkelstein, who called it "Bilanzstörung" (disturbed metabolic balance). It is brought about by a food mixture which is usually adequate as regards calories, but in which there is a faulty ratio between the food elements, that is, relatively too much fat and protein, and too little carbohydrate. In fat diarrhea it is the absolute amount of fat which is at fault, and the two conditions have a totally different pathogenesis. Balance disturbance is never seen when the food is breast milk, and indeed it may be cured by this food, although the fat content of breast milk is high.

In balance disturbance there is at first a standstill of weight, in spite of an adequate or even superadequate caloric intake, and later an actual loss, which may sometimes be large and

rapid, as it has been in this case. The stools contain a large amount of calcium soap, and the fat and calcium absorption is considerably lower than normal. It is likely, however, that this somewhat diminished absorption of fat and of calcium does not entirely account for the loss of weight, and other obscure factors are probably at work. There is a relative acidosis, with a consequent high ammonia excretion in the urine, which is, however, not severe enough to give the characteristic symptoms of acidosis.

The exact pathogenesis of the condition is not entirely clear, but enough facts are known to get a fairly accurate idea of it. When a food low in carbohydrate and relatively high in fat and protein is fed, the carbohydrate, especially if it be one (dextrin-maltose preparations) which is absorbed high up in the bowel, does not reach the large intestine. Thus there is no chance for even a slight fermentation there, and owing to the large amount of protein in the food, fermentative processes in the large intestine are inhibited, and a putrefactive bacterial flora is established. This, in connection with the large amount of calcium which is present in the food, produces an alkaline reaction in the large intestine. Peristalsis is slowed, and under these conditions, with a large amount of unabsorbed fatty acid and calcium present in a sluggish bowel, excellent opportunity is offered for the formation of insoluble calcium soaps. The stools become light in color, because under the influence of putrefaction the colored bile pigment bilirubin is reduced to the colorless hydrobilirubin. Bessau, who has written extensively on the subject, believes that this reduction is the most important and characteristic process in the morbid chemistry of the condition, and that the color of the stools is the best single guide to diagnosis, and as a check in the progress of treatment.

Treatment follows the suggestions offered by what we know of pathogenesis. The fat and protein should be reduced and the carbohydrate raised. It is not necessary to omit the fat entirely, as the primary trouble is not caused by fat. A carbohydrate should be used which is not so readily absorbed as a dextrin-maltose preparation, for the reason that it is desirable

to have a certain amount of unabsorbed carbohydrate residue in the large intestine in order to favor the growth of a fermentative flora, and to change about the putrefaction which is going on there. Lactose is best for this purpose, and most of the carbohydrate in the diet should consist of this sugar. It has been found by experience that these cases do better if a polycarbohydrate feeding is used, and it is always well to add moderate amounts of starch. It has also been found that the addition of a liquid malt extract preparation with a high maltose content is a valuable measure. The reason for this is not clear; possibly it acts by relieving the severe constipation which is always present. The carbohydrate in the formula should consist then mostly of lactose, in amount a little more than would ordinarily be used in feeding a normal baby, with the addition of 2 or 3 tablepoonfuls of barley or wheat flour, and 2 tablespoonfuls of a liquid malt preparation such as Maltine malt soup or Loeflund's Malt soup extract. The amount of milk should be reduced to between 1 and $1\frac{1}{2}$ ounces per pound of body weight. Usually half whole milk and half water, with the carbohydrate addition, would be a suitable formula.

In this particular case the treatment that was used was as follows:

Whole milk	21 oz.
Water	21 oz.
Lactose	6 level tablespoonfuls
Barley flour	2 " "
Maltine malt soup	2 " "

This gave about 55 calories per pound, almost exactly the same caloric value as the formula upon which the patient had been doing so poorly. It has, however, a totally different percentage composition, and this case is a very good illustration of the fact that in infant feeding more must be thought of than the caloric value of the food.

On this formula the baby gained 6 ounces the first week, and in three weeks he had gained a pound and three-quarters. He was kept on this feeding for about six weeks, after which the

amount of milk was increased and the malt soup omitted. Thereafter he was fed as any normal baby of his age.

Prophylaxis.—The prophylaxis of balance disturbance is important, as with correct feeding it should not occur. It was formerly believed that protein was difficult of digestion, and much smaller amounts of it were used in the once popular cream mixtures than in the now almost universally used whole milk mixtures. With the old feeding the concentration of milk, and hence of calcium and of casein, was kept low, and the deficiency of calories was made up by adding cream. On such a feeding balance disturbance was unlikely to develop. It is now known that the average normal infant can thrive while taking much greater concentrations of milk, and at present even very young babies are fed amounts of protein which would have seemed very large to the older pediatrists. This is well enough, provided it is not overdone, and when feeding babies on simple milk dilutions one must always bear in mind the ratio between protein-calcium and carbohydrate. If the baby is hungry it is a temptation to keep on increasing the amount of milk without reference to the carbohydrate, as was done in this case. As a matter of fact, the protein need of an infant is not very high provided the calories are well covered by carbohydrate and fat. With whole milk mixtures, in almost all cases, the baby is given considerably more protein than he needs for growth and for "wear and tear," and the excess is used for fuel.

The commonly accepted view at present is that $1\frac{1}{2}$ ounces of milk per pound of body weight amply covers the protein needs, and that it is never well to use more than 2 ounces per pound. This would give from $1\frac{1}{2}$ to 2 ounces of protein per pound, which is probably far above the actual minimum needs. There is very little accurate work on record to determine what this minimum may be. The only really scientific attempt I know of is by Langstein (Beiträge zur Physiol. u Pathol. des Kindesalters, 1919). He found that a liberal allowance for growth plus "wear and tear" during the first six months was about 7 grams of protein per day, which would correspond to only about $\frac{1}{2}$ pint of milk. This of course does not mean that it is desirable to feed

a baby as little milk as this per day, but it does show that his actual need for protein is not at all high, and that there is no danger of giving a baby too little protein in any ordinary milk mixture that would be used. There is more chance of giving too much, and a good rule to follow is never to give more than 2 ounces of milk per pound of body weight, and usually to keep well below this in feeding babies over six months of age.

CLINIC OF DR. EDWARD S. EMERY, JR.

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THE SIGNIFICANCE OF SO-CALLED CONSTIPATION

CONSTIPATION may seem to be a trite and commonplace condition on which to spend time. It may be because of this fact that so little attention is paid to it with resulting inaccurate diagnoses and ineffective treatment. By constipation is meant a condition in which the bowels fail to move or else move inadequately. Since the days of the ancients it has been associated with the thought of a failure of the body to rid itself of waste material, the accumulation or retention of which must necessarily be harmful. The problem of auto-intoxication is as old as the history of medicine. If the problem was only one of ridding the body of its lower intestinal contents the common practice of accomplishing that process by the simple expedient of giving a cathartic on the mere complaint of "constipation" would be justifiable.

Constipation is really more than this, however; for it is concerned with the principles underlying the workings of the gastro-intestinal tract. In one sense it has to do most intimately with the colon. With the increasing interest being attached to this organ anything concerned with its function is worthy of careful attention. The question of how the bowels act has to do with physiologic and pathologic processes occurring in the whole intestinal tract from the mouth onward. It is from this point of view rather than whether a patient moves his bowels every day or every other day that the subject deserves study. With more attention to this subject many of the erroneous ideas concerning the gastro-intestinal tract will be easily corrected.

A consideration of the subject requires first of all a careful definition. What constitutes inability to move the bowels or an insufficient action of the bowels? The standard must depend upon what occurs in the average normal individual as opposed to that in the abnormal. Under normal conditions material collects in the colon from the small intestine in a liquid condition, and as it is gradually propelled along the colon fluid is absorbed. At the time of dejection the fecal content has lost enough fluid to hold its shape and yet be easily molded. The consistency of a stool, therefore, is the result of two physiologic processes going on in the colon—motility and absorption. It follows that if motility is increased so that the normal or usual amount of absorption cannot take place the stools will be softer than normal. Conversely, where the motility is decreased, there is a greater chance for absorption to occur and the stools will be harder than normal.

On this basis a constipated person is only one in whom the stools are harder than normal; for how can it be possible for material to remain in the colon without undue absorption occurring, unless one assumes an inhibition of the process of absorption, and of this there is no evidence? The idea held not alone by laymen that a person may have inadequate evacuations although the stools are soft does not coincide with what is known. Of course, the occasional case in which scybalous masses become stuck in the colon and liquid material is squirted past the obstruction does occur. But this is a special condition that must be watched for, just as an obstruction due to a carcinomatous growth or a tuberculous constriction must be kept in mind and ruled out.

Keeping in mind what constitutes evidence of faulty evacuation let us consider a few cases which have been previously diagnosed and treated for constipation.

C. J. F., male, fifty-five years, was referred to me for intestinal trouble. He was complaining of fatigue and general debility, more marked for the previous nine months. He said that he had always been constipated, was troubled with considerable flatus, and felt that his complaints were due to auto-intoxication.

For years he had taken cathartics almost daily and about once a week would take a severe purge "to clear himself out." Physical examination revealed a somewhat sallow, underweight individual of the Stiller habitus. The abdomen was protuberant and suggested considerable ptosis. Otherwise the physical exexamination was negative. *x*-Rays of the gastro-intestinal tract showed only an atonic intestinal tract with marked ptosis and redundancy of the colon and some gastric retention. Other laboratory tests were essentially normal.

He was asked to stop all catharsis and was given a diet high in residue and chemical stimulation by means of the coarser vegetables and fruits. As the stools were quite hard, rather than increase his residue he was given a moderate amount of mineral oil, averaging about a tablespoonful a day, and by this means he was able to have daily movements without discomfort.

This case required more than the usual amount of alimentary stimulation to keep the bowels moving, and even then the stools were hard. It represents, therefore, a case of true constipation. Of the ptotic, asthenic type, his colon is large, long, low, and redundant. The gastro-intestinal tract shows a tendency toward atony and sluggishness as shown by the retention of barium in the stomach and the slow passage of the barium column. This, together with the great opportunity for absorption in so long a colon, explains the difficulty in getting any but hard stools.

The second case, E. J. M., Med. No. 26,152, is a widowed American woman, seventy-two years of age. Four years ago she had a gall-bladder operation. Following this she had been warned against becoming constipated. She had taken increasing quantities of cathartics until at the time of observation she was taking a cathartic daily. She had been having much abdominal distress of the functional intestinal type, which was her reason for seeking medical advice. Physical examination was essentially negative.

It required considerable persuasion to have her stop cathartics, as she said that her bowels would never move without help.

However, she finally agreed to eliminate cathartics for one week, at the end of which time she was to report. With this régime her bowels failed to move for two days. Since then she has had two to three mushy stools a day, and although on a bland diet her bowels are still very active.

This patient represents the individual who is thought to be constipated because the bowels are never given an opportunity to move by themselves. After the colon has been thoroughly emptied it may take two or three days for a sufficient amount of material to accumulate for a movement to occur without help. It usually happens, as in this case, that if a patient goes a day without a dejection he or she becomes worried. If a second day passes without results the patient becomes alarmed. A cathartic will then be taken at a time when the bowels are about ready to move, and would do so if given a little more time. In some cases it may take three or even four days before the bowels are ready to move. Once started there will be no trouble, provided judgment is used in prescribing the diet.

The third case (C. L. T.) is a young woman, eighteen years old, who came for constipation. She had been troubled with indigestion since a child, and at the age of nine had an appendicectomy for an acute abdominal pain. She continued to have indigestion, and was bothered almost constantly with a great deal of constipation. The family physician had prescribed many kinds of cathartics without success. The patient took a cathartic about three times a week. If, however, she took no cathartic her bowels would not move for four or five days. Finally her physician advised a ventral suspension of the uterus, on the grounds that the constipation was probably due to the somewhat retroflexed organ.

Physical examination and laboratory tests revealed a perfectly healthy and normal young woman. A brief period of questioning developed the fact that the patient had many likes and dislikes as to food. She ate a moderate amount of fruit, but practically no vegetables, her diet consisting for the most part of bland food.

On stopping her catharsis and taking three helpings of vegetables and two fruits a day, she had daily dejections and her distress disappeared.

This girl's bowels had not moved because they received no alimentary stimulus to make them move. There was nothing wrong with the intestinal tract. Given a normal stimulus the bowels moved perfectly normally. This is typical of many cases that are being treated for constipation, in which the patient's bowels are not moving simply because there is too little stimulus in the diet to cause them to move. It represents the indifference that is manifested by many of the profession to this condition, and the possible wrongs it may entail. To have allowed this girl to undergo a laparotomy would obviously have been inexcusable.

The next case (H. W.) is a man seventy years old. He came to the office with the request that I suggest some cathartic which would make his bowels work. He had suffered from "dyspepsia" for from twenty to thirty years, which was due, he said, to "inadequate elimination." Having started with mild laxatives he had gradually to increase the amount and severity of the drugs. In late years he had been to several physicians, each of whom had given different and supposedly stronger cathartics or copious irrigations. After a short while these means ceased to have any effect, so he came to see what I had to offer. At this time he was taking mineral oil and some 2 or 3 A. S. and B. pills or alophen pills, which would give him a daily movement, but which was inadequate he said because of the small amount of the evacuation and the lack of relief which he experienced. Physical examination and laboratory studies were negative in relation to his complaint. Explaining that I wished to learn the response of his intestine to an ordinary diet I asked him to stop his cathartics, take three vegetables and one helping of fruit a day, save all his stools, and report in a week. As a result of this week's trial he returned loaded with stool specimens. He had been having one or two stools a day, mushy almost watery in consistency. When the mechanism of the gastro-intestinal tract was

explained to him, and that it was impossible for him to be having an inadequate elimination, he was quick to catch the idea. Ultimately his diet had to be reduced to one adequate for a case of diarrhea before it was possible to obtain a normally formed stool. It was weeks before he could take a diet containing an average amount of stimulus in the form of vegetables or fruit without producing loose stools or distress. As the excessive irritability of the colon subsided, under a non-irritating régime, his "dyspeptic" symptoms gradually decreased.

This is typical of another type of case which is not infrequently seen, namely, that although the bowels are moving daily they are thought not to be moving enough. This patient had been treated for his symptoms of indigestion by many physicians over a period of years on the basis of the patient's statement that he was constipated. Some had given him a bland diet and increased the amount of catharsis. Others had given him a raw fruit and vegetable diet and decreased his catharsis. But no one had given attention to the total amount of stimulation applied. Most of them had never examined his stools or questioned him about them. The one or two who did examine his stools never suggested the fact that he could not be constipated.

One must conclude, therefore, that either these individuals did not know anything about the physiology of the intestinal tract or that they did not try to find out what the matter was with the patient.

Of these 4 cases, therefore, only 1 was truly suffering from constipation in the sense that the intestinal tract was actually sluggish in its response to stimulation. In one case the bowels did not move without cathartics, because they were given no adequate stimulus in the way of food; one because the patient gave the bowels no opportunity to move naturally, and one because of an inaccurate idea of what constituted a normal evacuation. From a strictly definitive standpoint two were having diarrhea rather than constipation.

I have discussed these 4 cases to show how the term "constipation" is used to cover a variable condition, namely, the response of the intestine to the stimulus it receives. Since the activity

or lack of activity represents the end-result of the various processes occurring in the whole intestinal tract it necessarily assumes an important place in the study of the gastro-intestinal tract. It is, therefore, important to know whether the patient's intestinal tract is in fact more active or less active than normal. Having ascertained this fact, one must return to the question of how much stimulation the intestine is receiving before deciding whether the tract is responding in a normal manner. In most cases it will be found that the intestine behaves normally if treated in a normal manner. Only those intestines which respond abnormally have an abnormal condition or conditions in the tract. But one cannot hope to master the puzzles of the system unless one keeps in mind simple concepts of physiology. Moreover, the cases discussed represent the careless way in which many patients with gastro-intestinal complaints are studied and handled, not alone in the care of the individual, but in the investigation of the physiology of the tract. It is due to this fact that one may be led into many false channels of reasoning.

Thus to report the result of bacteriologic studies on the intestinal tract, on the basis of constipation, is to give no adequate idea of what is actually being accomplished. If changing the flora of the intestinal tract has influenced bowel movements it has done so by influencing stimulation of the tract. One would like to know what the actual stimulation was before and after changing the flora. If an organism is introduced which causes marked stimulation on a bland diet, it is questionable whether the patient has not been harmed rather than benefited. Most studies of this kind do not give data sufficient to enable the reader to draw conclusions.

Then again the question of auto-intoxication is thought to be closely bound up with the presence or absence of so-called constipation. Space does not permit a discussion of this subject, and it is outside the purpose of this paper. It may be pointed out, however, that there are two explanations of the so-called symptoms of constipation. Some favor the idea of an absorption of intestinal products from the intestinal tract; and some a

mechanical basis for the symptoms. Whether auto-intoxication can occur I am unable to say. In the cases coming to my attention in which a diagnosis of auto-intoxication had been made there has been no adequate reason to assume that it exists. The burden of proof is on those who diagnose auto-intoxication to prove scientifically and beyond a doubt that it can occur. Such statements, as the one that the cecum is the cesspool of the body, though catchy, implies a condition which is not justified by what we know, and leads to many misunderstandings and harm.

The presence or absence of a condition called constipation is the result of the entire physiologic processes of the intestinal tract, both chemical and mechanical. As such it demands the interest, care, and attention of the medical profession in a way it has not received. With the advent of the *x*-ray there has been a tendency to take the easiest way out. The teaching of some that the gastric analysis and other such methods of study can be eliminated has resulted in not only losing the aid which these can give if one knows how to use them, but has led to an increasing carelessness in the investigation of gastro-intestinal problems, which is very unfortunate.

CLINIC OF DR. ROGER I. LEE

NEW ENGLAND DEACONESS HOSPITAL

THYROID DYSFUNCTION AS A CAUSE OF FEVER

THIS patient was first seen in March, 1925, at the age of forty-one. Her family history is relatively unimportant. She thought she was a strong vigorous woman until October, 1922, when she began to have afternoon temperatures of 99° to 100° F. She had various digestive disturbances of rather indefinite nature. At one time there was a certain amount of cough. On the basis of the fever, certain signs in the chest and *x*-ray findings of a definite deviation from normal in the left upper lobe, a diagnosis of pulmonary tuberculosis was made. Although her general condition continued good the fever persisted. Finally she went to a sanitarium for the tuberculous under very competent advice. The opinion there was that she did not have active pulmonary tuberculosis. When she got away from the sanitarium the usual procedure was that her physicians would find that she had fever, that she had curious signs in her chest, and a positive *x*-ray for tuberculosis, and she would be urged again to return to the sanitarium. She finally spent a year largely in bed. A chart during that time showed that her afternoon temperature was often 99° F. and often 100° F., and a pulse of 50 to 60.

She was referred to me in March, 1925, for an opinion to see if something else besides tuberculosis could be discovered. There was the usual search for a focus of infection. The *x*-rays showed negative sinuses, essentially negative teeth. Catheter specimen of urine was sterile. Repeated examination of the stools showed an occasional leukocyte, but no macroscopic pus. Ordinary physical examination was negative, except for the

signs of thickened pleura at the left base. Gastro-intestinal x-rays showed a good deal of gas in the terminal ileum. Basal metabolism was taken several times with an average of minus 20.

Under as carefully controlled conditions as possible she was given thyroid beginning with $\frac{1}{10}$ grain twice a day. This was increased until she got up to 1 grain a day, when there was an absence of temperature. With the omission of the thyroid medication the temperature returned.

On account of the rather indefinite but persistent abdominal symptoms, and because the patient had been a year in bed, and because she wanted to have everything done at this time, an exploratory laparotomy was decided upon. This showed a normal appendix, which was removed; normal stomach, gall-bladder, and pelvis. The cecum was very large. There was an uneventful recovery from the operation.

The experiment of leaving off the thyroid was tried a number of times. When the thyroid was omitted the temperature went up to 99° F., there was a feeling of lassitude, and there would be a fall in the basal metabolism from minus 10 to minus 20. The administration of $1\frac{1}{2}$ grains of thyroid six days a week and 3 grains once a week, was enough to eliminate the fever. Basal metabolism done in June, 1925, was minus 1; in March, 1926, plus 0.2. She is still taking her thyroid and apparently requires just over $1\frac{1}{2}$ grains a day. Whenever the thyroid is omitted she has a temperature of 99° to 100° F. Her pulse has constantly ranged between 54 to 66, even with the fever.

A subnormal temperature with hypothyroidism is, of course, the rule. I am not familiar with hypothyroidism with fever. Moreover this fever is definitely removed by the administration of thyroid in this case. A striking feature was the association of the very slow pulse with the temperature. The case, of course, is not a case of myxedema. There is probably no organic disturbance of the thyroid gland. We do not know the mechanism by which the temperature is produced when the basal metabolism is low, or the temperature returns to normal with the normal basal metabolism, with the administration of thyroid substance.

Most internists feel that at the present time thyroid medication is far too frequently given. However in certain cases it is entirely justifiable to administer thyroid substance. The mere presence of a low metabolic rate is not an absolute indication for the administration of thyroid. In this particular case, more impressive by far than the metabolic rate and its change under the administration of thyroid substance, was the alleviation of the conspicuous symptoms of temperature by thyroid administration. The experiment was tried many times and there was a constant correlation between the temperature and thyroid administration. Cases of this sort are probably rare. Cases of persistent temperature of a year or more with a pulse of 60 or under must be rare. It is probably unjustifiable to give thyroid in such cases, even with a low basal metabolic rate, until a thorough search has been made for possible foci of infection. In this particular case no focus was found and the abdomen was opened because it seemed possible that there might be some focus of infection within the abdomen.

The patient now considers herself well and is well symptomatically as long as she takes thyroid. Her chest signs by *x*-ray remain unchanged. Therefore we are compelled to assume that rarely hypothyroidism is associated with fever.

CLINIC OF DR. CHANNING FROTHINGHAM

PETER BENT BRIGHAM HOSPITAL

A CASE OF CORONARY THROMBOSIS

THROMBOSIS of some branch of the coronary arteries with subsequent infarction of a part of the cardiac muscle is either becoming more frequent in this community or else the medical profession is more alert in making the diagnosis. With the increasing number of cases that are diagnosed it has become apparent that the condition may present a great variety of symptoms and physical findings. Also, the course of the disease and its outcome is by no means the same in all cases. It is therefore of interest to present cases which show any unusual features or which have offered an opportunity for special study, so that the profession may be acquainted with all the variations of this disease.

It is becoming more apparent that this disease occurs at very different ages and that it not only may occur in elderly people with marked arterial changes, but also in relatively young people in whom there has been no evidence of any appreciable degree of arterial disease. It is well known that the condition may lead to sudden death within a few minutes or hours after the onset of the attack, or that death may occur after some days, due to rupture of the heart muscle in the area rendered necrotic by the shutting off of the blood-supply. Sudden death may also occur some days after the infarction without any appreciable new developments in the infarcted area. In other instances repair by scar tissue formation takes place in the infarcted area and the individual is left with a heart that is more or less seriously damaged. In still other cases apparently repair may take place without any evident serious injury to the heart

muscle, so far as its ability to perform its function is concerned. These variations in the outcome undoubtedly depend upon the extent of the infarcted area in the cardiac muscle.

In addition to changes in the cardiac muscle itself, which affect the strength of the ventricular beat, injury may occur to the conduction system of the heart so that variations in rhythm will be the outstanding symptoms of the disease.

At the present time there is little evidence to show why thrombosis occurs in these coronary vessels. There seems to always be an existing arterial sclerosis, but it is not clear whether the thrombosis is caused just by the changes in the arterial wall or to some additional unknown factor. It is also not clear why a patient should have the coronary arteries especially sclerosed without marked sclerosis in vessels elsewhere. Although syphilis is a common cause for arterial changes in different parts of the body, especially in the aorta and heart, it seems fair to say that syphilis is not a necessary factor for the production of coronary thrombosis, since there seem to be many cases of cardiac infarction in which syphilis can be satisfactorily excluded.

The case which is about to be described is of interest in that the thrombosis of the coronary artery occurred in a relatively young man without any previous suspicion of vascular disease. It is also of interest because the infarction produced much more disturbance temporarily in the rhythm of the heart than in its ability to do its work. It was also possible to obtain a series of electrocardiographic studies during the stages of the illness in which the rhythm was upset. Furthermore, at the present time the patient is apparently free from symptoms and there are no signs of permanent damage to the heart as a result of the infarction. The patient has not as yet tested out the ability of his heart to respond to pronounced physical exertion. It is also amusing to speculate as to whether the extreme heat at the time of the patient's illness might have been a factor in the production of his thrombosis.

A male, aged forty-five, who had been feeling perfectly well, was suddenly taken ill about noon on July 22, 1926, while

riding in a taxicab from the North to the South Station in Boston, Mass. It was an exceedingly hot day, the temperature registering 99° F. at midday. The patient had not been undertaking any special muscular activity just preceding the attack. He suddenly had a feeling of nausea with oppression in the epigastric region and over the lower portion of the sternum. At the same time there was a sensation of numbness with some pain going down both arms, which localized chiefly in both wrists. He broke into a cold perspiration, but succeeded in reaching his office, where he lay flat upon a sofa but was very restless. Except for the above-described sensations he complained of no symptoms.

In his past history there was a story of erysipelas as a child, associated with vaccination against smallpox. He had had chickenpox, mumps, measles, rubella, and scarlet fever. At about the age of twenty he had had a urethritis which cleared up quickly and completely. At the age of thirty-three, because of the possibility of beginning deafness, he had his tonsils removed. He has had no other operations. In 1920 he had a bronchopneumonia, from which he recovered without complications.

In March, 1925, he had considerable pain in the right shoulder, which sometimes extended down the right arm and at other times went up into the neck. This was worse when he awakened in the morning and did not seem to be associated with physical exertion. There was no limitation of motion or evidence of bony abnormality, as shown by the *x*-ray, in the right shoulder-joint. The diagnosis of bursitis was made at that time and rest for the shoulder-joint advised. Despite a fairly careful attempt on the patient's part to give the shoulder-joint rest, the pain continued to bother him through the summer and autumn of 1925, and was finally relieved by osteopathic treatment during the winter of 1925 and 1926. This pain is described at some length because of the possibility that this might be looked upon by some as cardiac pain. In view, however, of the fact that it did not seem to be related to exercise and was eventually cleared up by osteopathic manipulations, it seems reasonable to con-

sider that it was not cardiac in origin. On account of this pain a careful physical examination was made in March, 1925, and nothing abnormal was found. The blood-pressure was reported as normal. The urine was free from albumin or sugar, and there were no pus-cells, blood-cells, or casts in the sediment. The hemoglobin was 100. The blood-smear was negative. The Wassermann reaction in the blood-serum was negative. There was nothing else in the past history of importance.

His father died at the age of sixty-four of what was probably a coronary thrombosis, although at that time it was called acute indigestion. His mother died at the age of seventy-two of a cerebral hemorrhage. She had two or three previous hemorrhages into the cerebrum. Otherwise the family history seems unimportant.

The patient was seen by the writer within half an hour of the onset of the pain. At that time the patient showed definite pallor with coldness of the extremities and cold sweat upon the body, head, and extremities. He was quite restless and continued to complain of an oppressed feeling beneath the sternum and pain in both wrists. He was able to lie flat. The radial pulse was of small volume and variable in rhythm. At times it was regular and not rapid. At other times it was slow and irregular. At still other times there was a definite coupling of the beats, even at the wrist. He continued to feel nauseated and attempted to vomit, but nothing was returned from the stomach. A complete physical examination was not made at that time. He was given $\frac{1}{6}$ grain of morphin subcutaneously, and this was repeated in fifteen minutes. Following the second injection of morphin the discomfort in the chest subsided considerably and the pain disappeared from the arms. The cold perspiration gradually subsided, but the heart action continued to show the same variations in rhythm. He was then moved in an ambulance to the Massachusetts General Hospital.

The diagnosis was made at this time of thrombosis of the coronary artery and this seemed to be further substantiated by the subsequent course of events, for the patient developed a mild febrile reaction which lasted for a few days without other

apparent cause, and this febrile reaction was accompanied by a mild leukocytosis. In addition, irregularities in the cardiac

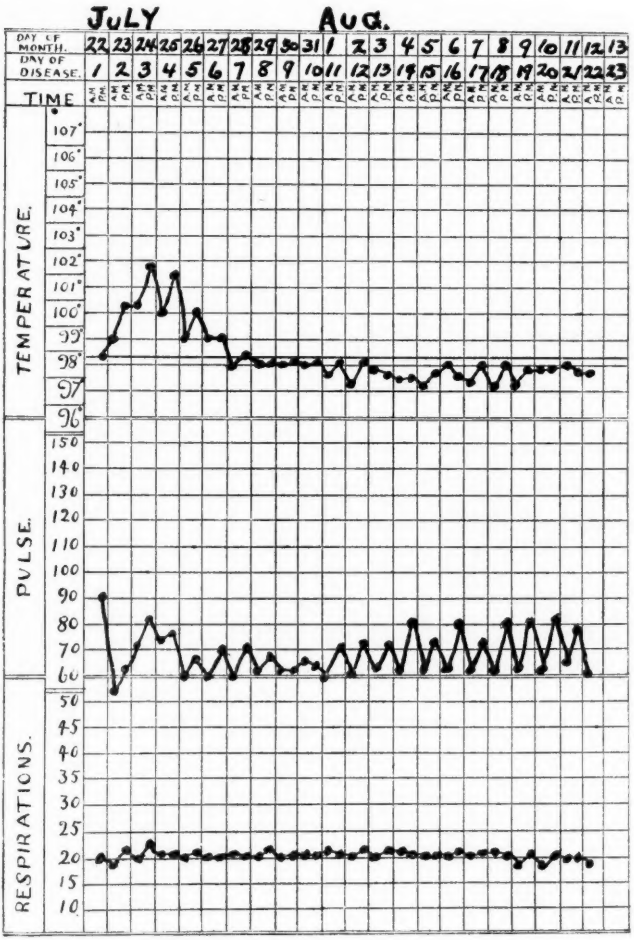

Fig. 161.

rhythm appeared off and on for several days, and then the regular rhythm returned permanently. Also, variations from

normal in the ventricular complexes of the electrocardiograms indicated that some disturbance had been going on in the heart. There was also no other condition found on careful study which might account for the symptoms and signs. The chart on page 1361 shows the course of the temperature, pulse, and respiration during his stay in the hospital.

After the pain first subsided in his wrists it did not return; neither did the marked oppression beneath the sternum return. For the next day or two there was slight discomfort in the epigastrium with some loss of appetite. Otherwise the patient remained free from symptoms for the rest of his stay in the hospital.

On July 23, 1926, the day following the onset of the illness, his physical examination was essentially negative, except for

Fig. 162.

the variations in the cardiac rhythm and the character of the heart sounds, which were rather faint. The urine was essentially normal. The white count was 10,400. Blood Wassermann negative. The blood-pressure was 125 systolic over 110 diastolic. No other abnormal physical signs developed, as the course of the disease continued, and therefore the interest in the case centers about the action of the heart. Except for the faintness of the heart sounds, and the variations in the rhythm, nothing developed in the heart which showed up upon physical examination, and the disturbance in the heart is best described by the series of electrocardiograms that were taken.

On the afternoon of the day in which the illness began, namely, July 22d, an electrocardiogram showed complete dissociation between the auricles and the ventricles. The auricular

rate was 115 and the ventricular rate 40. Unfortunately, due to trouble with the machine, the only lead which could be taken was Lead II (Fig. 162).

No electrocardiogram was taken on the next day, but the variations in the rate and rhythm suggested that at times a normal rhythm was going on and at other times the heart-block at the auricular-ventricular node persisted. On July 24, 1926 an electrocardiogram showed a regular rhythm with a prolonged P-R interval, and the same condition was found in the

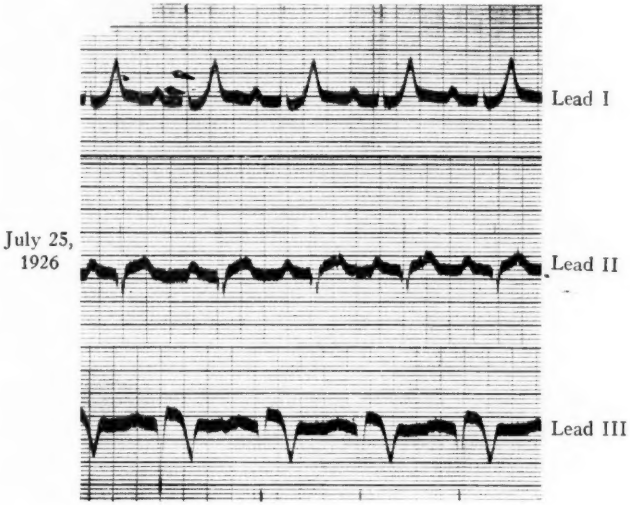

Fig. 163.

electrocardiogram taken on July 25th. This latter is reproduced in Fig. 163 and shows evidence of left ventricular preponderance, a normal rhythm with both the auricular and ventricular rates 80, and a prolonged P-R interval of 0.25 seconds. In addition, the T wave in Lead I is high and the T wave in Lead III is deeply inverted.

On the next day, July 26, 1926, four days after the onset of the illness, the electrocardiogram again showed complete auricular ventricular dissociation. This time the auricular rate was

78 and the ventricular rate 65. In addition there was a high T wave in Lead I and a deeply inverted T wave in Lead III, with a somewhat unusually rounded T wave in Lead II. It also showed evidence of left ventricular preponderance.

With this reappearance of the abnormal rhythm there were no new subjective symptoms. On the following day, July 27, 1926, the heart had returned to a normal rhythm, but there was still a prolonged P-R interval of 0.22 seconds. The T wave in Lead III was also still inverted. On the next day, July 28, 1926,

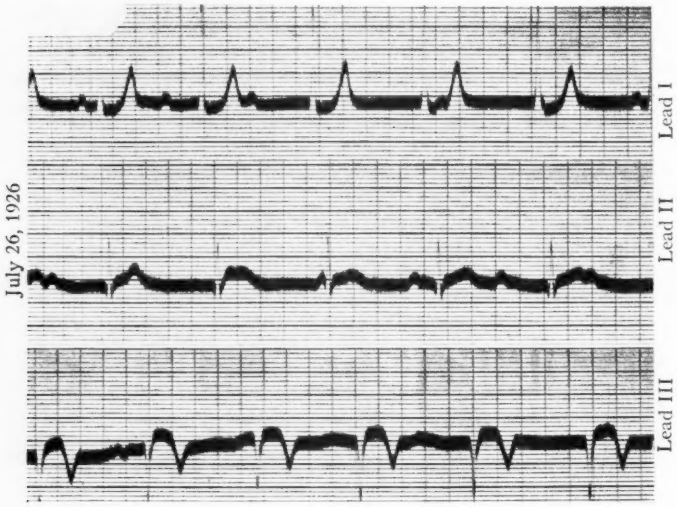

Fig. 164.

the normal rhythm persisted, but the P-R interval had shortened still further until it was 0.2 second. On July 30, 1926 the P-R interval had returned to normal, and the only abnormality in the electrocardiogram was the inverted T wave in Lead III and the evidence of left ventricular preponderance. The rate was 70.

From this time on no further abnormalities developed in the electrocardiograms, and the ones taken on August 4, 1926, and later on September 21, 1926, showed a normal complex with the exception of the inverted T wave in Lead III, and evidence of

left ventricular preponderance. From these electrocardiograms it is evident that some injury occurred to the bundle of His, which for a time completely interfered with its function and then gradually allowed the function to return, at first imperfectly and finally in a normal manner. They also showed evidence of injury to the heart by the inverted T wave in Lead III. Also they bore out the point which was made in the *x*-ray studies later of an hypertrophy of the left ventricle.

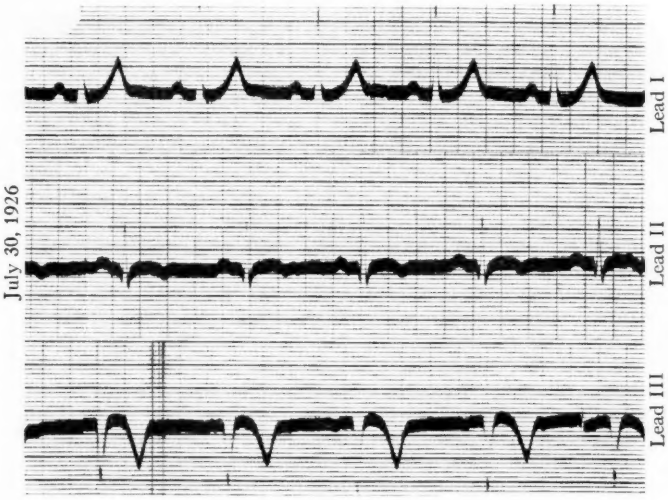

Fig. 165.

While the patient was in the hospital, on August 12, 1926, an *x*-ray examination was made of the heart by Dr. George W. Holmes, and it showed that the heart shadow was definitely increased in size. The increase was most marked to the left in the region of the ventricle. Pulsation was indistinct and the heart appeared flabby. The supracardiac dulness was increased, the aorta was wide in both the anteroposterior and lateral views. The diaphragms were high, which may have accounted in part for the increased transverse diameter of the heart shadow. The measurements on a 7 foot plate showed the right border

5 cm. from the midline, left border 11 cm. from the midline, total transverse diameter 16 cm., great vessels 8 cm., internal diameter of the chest 26.5 cm. Dr. Holmes summarized with a statement that the findings were those of enlargement of the heart with dilatation of the aorta. These findings by *x*-ray of a slight enlargement of the heart and aorta had not been picked up on careful physical examination a year before, but they were so slight that it seems quite likely that they would have been overlooked in a routine physical examination.

Following the patient's departure from the hospital on August 12, 1926, he continued his convalescence at his home and very cautiously increased his activities without a return of any of the old symptoms or the development of any new ones. During this period the first heart sound was of rather poor quality, and the blood-pressure, which by August 1, 1926 while he was still in the hospital, had dropped to 115 systolic over 80 diastolic, continued to be low, and on August 12th the pressure was 110 systolic over 70 diastolic. By September 21, 1926 the patient had returned to a fairly normal life, except that he avoided any form of exercise which made him short of breath or accelerated the pulse rate, and he had not returned to business. He was free from symptoms except that he thought he possibly became a little short of breath upon moderate exercise, which ordinarily would not have bothered him. On that date the physical examination of the heart was essentially negative, the action was regular, the heart sounds seemed to be of good strength, and there were no murmurs. As mentioned above, the electrocardiogram on that date showed no abnormality except for left ventricular preponderance and an inverted T wave in Lead III.

The patient continued to return gradually to his normal life without active exercise. He took up business again and remained free from symptoms. On December 16, 1926 the physical examination was still essentially negative. An *x*-ray of the heart taken at that time by Dr. Merrill C. Sosman showed moderate cardiac enlargement to the left fluoroscopically. The beat was regular, slow, and showed a good auricular ventricular

differentiation, and the aorta appeared somewhat dilated. The measurements in the 7 foot plate showed the great vessels 6.5 cm., the right border 4.8 cm. to the right of the median line, left border 10.9 cm. to the left of the median line, transverse diameter 15.7 cm., and the internal diameter of the chest 28.2 cm. At this time, therefore, the patient still showed some slight enlargement of the heart and aorta, which probably were present before the acute illness in July, 1926, and which did not change appreciably as recovery took place. Just what was the cause of the slight changes in the heart and aorta in the patient is not clear. They do not seem to be the result of luetic infection or previous hypertension. They suggest localized arterial disease of obscure origin in the heart and aorta in an otherwise healthy individual. Until the cardiac attack these changes had produced no symptoms, nor had they even been suspected.

This case, therefore, presents an instance of a thrombosis in a branch of the coronary artery which supplied the muscular tissue in or about the bundle of His. It would appear as though a small area of the heart only had been infarcted, because of practically no disturbance to the carrying on of the circulation. The injury apparently was limited chiefly to the conduction system of the heart. The case is of interest in showing the appearance of heart-block, followed by a normal rhythm with the reappearance of the heart-block and a final return to normal rhythm over a period of several days. It is also of interest to see the gradual transition from complete inability of the bundle of His to function back to normal function with variations in the time it took impulses to pass along the bundle. It is interesting to speculate on how much physical exertion this patient can undertake in the future without production of cardiac pain. Up to the present time he is doing more and more in the way of moderate exercise, such as walking and shooting, without symptoms. Could there have been any relation between the development of the coronary thrombosis and the extreme heat that was present on July 22, 1926?

CLINIC OF DRS. W. RICHARD OHLER AND LOUIS J. ULLIAN

BOSTON CITY HOSPITAL

MILD HYPOTHYROIDISM—PERSONAL OBSERVATIONS

DURING recent years basal metabolism tests have become more and more a part of a routine clinical study. As a consequence, basal metabolic rates have been reported in a great many conditions. Heretofore we were taught to associate the basal metabolism primarily with the thyroid gland. This is comprehensible when we realize that the thyroid's chief function is the regulation and control of the basal metabolism, *i. e.*, body heat production. Accordingly, it is in two definite pathologic states of the thyroid—hyperthyroidism and myxedema or cretinism—that we encounter abnormal rates of the basal metabolism. It is in the former—a condition due to either an increased or an altered thyroid secretion—that we find the increased rates, and it is in the latter—a condition due to a decreased thyroid secretion—that we find lowered rates. The more recent wide-spread use of the basal metabolism test has resulted in a changed or changing conception of metabolic disorders. It is known, for example, that increased basal metabolic rates are found in the various leukemias, in Hodgkin's disease and in febrile conditions, and that lowered rates may be encountered in conditions resulting in marked cachexia and exhaustion. It is also apparent that slight changes in the basal metabolic rate, especially on the minus side of the so-called normal range, occur in a large group of patients who have not a complete picture of clinical myxedema, and yet who present a varied number of the symptoms and signs of some lowering of the body heat production. Such conditions are found with sufficient frequency to constitute a clinical entity. It is par-

ticularly with this phase of the problem that we are concerned in this report. Are slight or moderate reductions in the basal metabolic rate in the absence of definite clinical signs of myxedema or cretinism of any significance? The question is pertinent not only because of the frequency of slightly lowered rates in any metabolic clinic, but also because of the lack of unanimity in the interpretation of these results. In general, basal metabolism results are considered normal if they fall within a range of minus or plus 10 per cent. We are not willing to accept any such iron-clad limitation, especially in regard to the minus readings, because readings not as low as minus 10 per cent. are often significant. In other words, our inclination is to pay attention to all minus readings provided they are associated with any of the clinical signs of a decreased body heat production. In this connection it may be well to state that basal metabolic rates vary directly with the intensity of symptoms, and that it is only in the definitely well-established state of myxedema that all the symptoms of a low body heat production are present. The slightly and even moderately advanced cases more often do not show the complete clinical picture characteristic of myxedema.

The more important signs of a lowered body heat production are as follows: 1. Retarded mental processes, among which a failing memory and slow response to questioning seem more frequent. 2. Slow speech. 3. Huskiness or hoarseness of voice. 4. Easy fatigue with varied degrees of dyspnea. 5. Failing strength. 6. Lowering of the blood-pressure. 7. Retardation of the pulse rate. 8. Cool and dry skin with diminished to absent perspiration. 9. Dry scalp and hair. 10. Abnormal sensitiveness to cold. 11. Decreased appetite. 12. Tendency to increased weight. 13. Pallor, associated with secondary anemia. 14. Pale to blanched mucous membranes. 15. Decreased kidney and intestinal function. 16. Retarded menstrual cycle. 17. Puffiness, non-pitting of eyelids and extremities particularly, but may be general.

The patient who presents these symptoms to their highest degree has myxedema and consequently has a definitely lowered

basal metabolic rate. There are other patients, however, in whom many of the above symptoms are absent, and in whom the symptoms that are found are noted as being only slightly or moderately advanced. Such patients have only a slight reduction in the basal metabolism, the result very often falling between minus 10 per cent. and zero. In other cases the metabolic rate is only a trifle lower than the usually accepted normal range. Possibly these patients should be classified as cases of mild myxedema or, as already has been suggested, cases of hypothyroidism without myxedema. At any rate, such cases are sufficiently numerous to warrant investigation, paying particular attention toward determining whether or not they may have mild degrees of hypothyroidism. If this condition is found, treatment should be attempted with a view to raising the body heat production along with any other therapy that may be indicated.

The intent of this article is to record personal observations of patients who show some of the symptoms of a lowered heat production, and in whom the basal rate is only slightly or moderately reduced. The material used is drawn from the metabolic clinic at the Boston City Hospital and from private practice. Obviously, it is not possible to cite a large collection of cases, and only a few selected protocols are given—enough, we believe, to demonstrate how interesting the general subject is. Here it is fair to state that our observations are based on basal metabolic studies alone. Recently Lawrence and his co-workers at the Evans Memorial, Boston, have published observations tending to correlate basal metabolic findings with certain changes in blood chemistry and blood morphology.[1] Possibly it is too early as yet to draw any definite conclusions on this interesting phase of the subject.

In presenting the following cases some attempt has been made at classification or grouping. This is done primarily for purposes of discussion, appreciating fully how unsatisfactory classification in this particular subject is. Strictly speaking, all of the cases given below are cases of mild hypothyroidism except

[1] Boston Medical and Surgical Journal, vol. 196, No. 2, 43–50.

that in some certain other pathologic conditions predominate, as, for example, obesity and arthritis. However, rather than approach the problem from the angle of basal metabolism studies in, say, obesity or in arthritis or in any one of a number of pathologic conditions, we believe in a more direct attack. Given a case of obesity, are there any signs of hypothyroidism, or given a case of arthritis, is there anything in the history or physical examination suggesting a lowered basal rate? In other words, obesity, certain types of arthritis, secondary anemia of unknown origin, debility without evident cause, may often be symptoms of hypothyroidism. Our belief in the justification of such an approach to this problem is strengthened by the history of many patients who have been from one physician to another before the real source of the trouble was detected.

Case I.—M. J. S. Male. Age thirty-five.

First seen in October, 1924. Weight 240 pounds. Height 73 inches.

Past History.—During the past few years has put on weight rapidly. History otherwise unimportant.

Physical Examination.—Essentially negative. Blood-pressure 120/80. No evidence of anemia. Wassermann negative. Urine normal. Blood urea nitrogen 18.6 mgm.

Endocrine Symptoms.—Constipation, lack of ambition, easy fatigue.

Metabolism Studies.—October, 1924. Basal metabolism, minus 21.8 per cent.

January, 1925: Basal metabolism, minus 10 per cent.

September, 1925: Basal metabolism, minus 11.7 per cent.

March, 1926: Basal metabolism, minus 11 per cent.

During this year and a half the patient's weight has dropped from 240 to 209 pounds. He has refused to follow a prescribed diet, but has eaten sparingly of butter, sugar, candy, and rich pastries. Medication has varied from 1 grain of thyroid a day to $\frac{1}{2}$ grain every other day. He is still losing weight slowly and is in excellent physical condition.

Case II.—L. L. P. Male. Age twenty-four.

First seen in May, 1926.

Past History.—Has always been very heavy, and during the past three years has gone to 300 pounds and over. About three years ago some doctor gave him thyroid, which resulted in no noticeable change in his general condition. Nocturia two to four for some years. Dyspnea on slight exertion.

Physical Examination.—Aside from the marked obesity there was nothing remarkable.

Endocrine Symptoms.—Marked lassitude with extreme weariness and drowsiness during day; lack of appetite; easy fatigue.

The following is a brief resumé of this patient's basal metabolic studies and his clinical record:

May 29, 1926: Basal metabolism, minus 14.8 per cent. Pulse 68. Weight 301 pounds. Treatment: Thyroid, grain 1 daily.

August 4, 1926: Basal metabolism, minus 11.4 per cent.

August 11, 1926: Weight 301 pounds. No change clinically. Treatment: Increase thyroid to 2 grains daily. Patient also given fat-free diet containing approximately 1500 calories.

September 18, 1926: Weight 278 pounds. Pulse 68. Nocturia has disappeared. Feels much better, his lassitude and fatigue being much less marked.

October 16, 1926: Weight 267$\frac{3}{4}$ pounds. Pulse 64. States that he feels fine.

November 20, 1926: Weight 258$\frac{1}{4}$ pounds. Pulse 72. Taking 2 grains of thyroid daily. States that he never felt better in all his life.

December 18, 1926: Basal metabolism, minus 4.7 per cent.

December 29, 1926: Weight 254$\frac{3}{4}$ pounds. Pulse 80. General condition excellent.

Comment.—The above 2 cases may well be grouped as cases of obesity. In our experience about 20 per cent. of the cases of obesity seen in the clinic have a lowered metabolic rate. This lowering of the metabolic rate is not always below the so-called normal range, which has as its low limit minus 10 per cent. Regardless of this, however, we feel that the metabolic rate may

be definitely significant, even though the minus reading is not lower than 10 per cent.

In considering a case of obesity three questions present themselves:

First, is the case purely one of disproportion between food intake and energy output, that is, overeating?

Second, is the case purely one of endocrine dysfunction with resulting increased weight?

Third, is the case a combination of the preceding two conditions?

With the above questions in mind, it seems essential that basal metabolism studies should be done—if at all possible—in all cases of obesity, and that the result of these studies should be considered in connection with the clinical manifestations present. If there is no lowering of the metabolic rate, and there are no clinical evidences of a lowered body heat production, thyroid extract should not be given, as we have seen harmful results in several instances where this drug has been prescribed empirically. Very often a case that presents both clinical and metabolic evidence of a lowered basal metabolism will not lose weight on thyroid administration alone. If this condition is encountered, it is necessary to incorporate into the daily treatment diets which are fat free and slightly low in total calories. In our clinic we have employed an essentially fat-free diet containing approximately 1500 calories for a twenty-four-hour period.

Case III.—H. G. Female. Age thirty-nine.

A high-strung, nervous, intellectual type of individual who presented herself two years ago complaining of nervousness and fatigue.

Past History.—The usual childhood diseases. The patient seems to have been a rather sickly child, suffering from many minor infections, usually upper respiratory in type. In 1922 a diagnosis of duodenal ulcer was made. Patient has responded well to medical treatment and during the past two years has had but few gastric symptoms.

Physical and Laboratory Findings.—Slight pallor; blood-pressure 105/76; pulse rate 70; slight tenderness without spasm over the duodenum. Red blood count 4,200,000. Hemoglobin 80 per cent. Blood-smear shows a mild secondary anemia. Wassermann negative. Examination otherwise not remarkable.

Endocrine Symptoms.—Easy fatigue; an abnormal reaction to cold; low blood-pressure; coarse, dry hair.

Metabolism record and treatment:

January, 1925: Basal metabolism, minus 9.5 per cent. Started on thyroid, ½ grain a day.

March, 1926: Basal metabolism, minus 14 per cent. After the first test patient took thyroid for about three weeks. Improvement was marked and patient stopped the drug. She continued to feel well until about two months ago, when she began to feel a return of the old symptoms. Following the metabolism test in March, 1926, patient was given thyroid, ½ grain twice a day.

May, 1926: Patient much better. Feeling of fatigue gone. Living a very active social life. Refuses to have further tests for the present.

November, 1926: Basal metabolism, minus 15.8 per cent. Associated with the above metabolism result is the story of a return of symptoms, especially easy fatigue and an abnormal reaction to cold. Patient started once more on thyroid, ½ grain twice a day.

January, 1927: Patient responded well to thyroid given in November. Takes the drug off and on. Says she soon feels the lack of it if she goes without it for a few days. At present appears to be in excellent condition and refuses to have a metabolism check-up.

Comment.—The above case represents one of a fairly large group and will serve as an example of a class which we chose to call the high-strung, nervous, easily fatigued type. In this group the condition of hypothyroidism may not suggest itself at first. Patients of this type are often underweight, they are not mentally dull, nor do they appear physically inactive. On the other hand, in a social group they may be the most animated

individuals present, full of life and vigor. Such animation, however, is apparent rather than real—for after a few hours the patient is completely exhausted both mentally and physically. Thyroid therapy in this group has given uniformly good results—fatigue and nervous exhaustion disappear, patients often gain in weight and in a general way feel better and stronger.

Case IV.—S. P. Female. Age sixteen.

First seen in August, 1925.

Past History.—Usual childhood infections without serious complications. Takes cold easily. Menstrual function began at eleven and is normal.

Physical and Laboratory Findings.—Short, stocky type, slightly overweight. Slight lordosis. Physical findings otherwise normal. Wassermann negative. No evidence of secondary anemia. Non-protein nitrogen normal. Urine normal.

Endocrine Symptoms.—1. Complains of tired feeling in the arms and legs. Condition not related to exercise. 2. Feels sleepy all the time. Sleeps especially well at night, but not refreshed in the morning. 3. Very enthusiastic about her school work early in the year, but seems to be unable to carry things through. Apparently becomes both physically and mentally tired as the school year progresses. 4. At times very irritable without cause.

Basal metabolism studies and treatment:

August, 1925: Basal metabolism, minus 13.9 per cent. Patient started on thyroid, $\frac{1}{4}$ grain a day.

September, 1925: Basal metabolism, minus 12 per cent. Thyroid increased to $\frac{1}{4}$ grain twice a day.

November, 1925: Basal metabolism, minus 12 per cent. Thyroid increased to $\frac{1}{4}$ grain three times a day.

December, 1925: Basal metabolism, plus 1 per cent.

April, 1926: Basal metabolism, plus 4.8 per cent. Thyroid decreased to $\frac{1}{4}$ grain twice a day.

Since taking thyroid there has been a definite improvement in patient's symptoms. Parents are absolutely certain that thyroid medication has changed the patient's entire mental and

physical behavior, and they now look upon her as a normal child. She still takes from $\frac{1}{4}$ to $\frac{1}{2}$ grain of thyroid a day.

Case V.—R. C. Male. Age twenty-one.

First seen in November, 1926.

Past History.—Unimportant. In fact, unusually free of sicknesses.

Physical and Laboratory Findings.—Slightly overweight. Blood-pressure 100/70. Pulse 62. Physical findings otherwise normal. Wassermann negative. Very slight secondary anemia. Non-protein nitrogen 32 mgm. Urine normal.

Endocrine Symptoms.—Lacks ambition; starts things, but does not seem to have the ability to finish them; tires very easily, mopes around the house; does not seem to be especially keen about anything despite the fact that previously he was a wide-awake boy, fond of all kinds of outdoor sports.

Basal Metabolism Studies and Treatment.—November, 1926: Basal metabolism, minus 14 per cent. Started on thyroid, $\frac{1}{2}$ grain a day.

January, 1927: Basal metabolism, plus 0. Now taking thyroid, $\frac{1}{2}$ grain three days a week.

Since taking thyroid there has been a marked general improvement. Parents state that he is an entirely different boy.

Comment.—We have seen a number of young people similar to the two described above. As a class they are overweight and stocky in build. In the girls, menstrual disorders are common. Small doses of thyroid seem to have a beneficial effect, and where menstrual disorders exist, thyroid seems of benefit also. One wonders how many young people of high school or college age belong to a group of this sort.

Case VI.—R. Z. Female. Age forty-six.

First seen in April, 1926. For a few weeks previous to this she had been consulting various physicians because of stiffness and aching of the left knee with great difficulty in walking and going up and down stairs. She was told the condition was a rheumatic one.

Physical and Laboratory Findings.—Pallor marked; skin cool and dry; 30 pounds overweight; blood-pressure 98/80; pulse 88, of small volume and poor tension. Kidney function studies were negative. Blood-sugar (fasting) normal. Blood uric acid normal. Hemoglobin (Sahli) 75 per cent. Red and white blood-counts normal; blood-smears negative except for a moderate achromia.

Endocrine Symptoms.—Dry skin, increased sensitiveness to cold, fatigue on slight exertion, an increase in weight of 20 to 30 pounds during the past five years, hot flashes, amenorrhea past five years, low blood-pressure.

Basal Metabolism Record, Treatment, and Progress.—April 29, 1926: Basal metabolism, minus 11.8 per cent. Weight 157¾ pounds. Pulse 72.

May 5, 1926: Thyroid extract started, 3 grains daily.

May 26, 1926: Much improved. Strength better; can walk up steps normally; still some stiffness in knee. Started on 1500 calorie fat-free diet as there has been no loss of weight in the past three weeks.

June 1, 1926: Blood-pressure 112/72. Pulse 84.

August 3, 1926: Basal metabolism, minus 7.9 per cent. Has lost 7 to 8 pounds. Knee does not interfere with walking. Generally much better.

September 16, 1926: Feeling well. Has omitted thyroid past ten days on own initiative. Knee has been well. No fatigue on walking, not sensitive to cold. Blood-pressure 114/76. Pulse 78. Treatment: Continue with thyroid, 3 grains daily.

September 23, 1926: Basal metabolism, minus 12 per cent. Weight 139 pounds. Pulse 60.

October 9, 1926: Feels well. Knee essentially normal. Has lost about 20 pounds. Blood-pressure 114/74. Pulse 80. Treatment: Omit 1500 calorie diet.

October 29, 1926: Basal metabolism, minus 10.8 per cent. Weight 137¾ pounds. Pulse 70.

January 15, 1927: Knee is well. During past two weeks fatigue comes on more quickly and is tired on arising in the morning. Previous to this has felt very well.

January 21, 1927: Basal metabolism, minus 15.4 per cent. Weight 140 pounds. Pulse 62.

Comment.—The diagnoses in this case are as follows: Mild hypothyroidism. Mild secondary anemia. Menopause. Chronic arthritis. The important condition is undoubtedly the hypothyroidism. This case is representative of others we have seen where the chief complaint has been arthritis and where, due to certain clinical symptoms and signs, hypothyroidism was suspected. In these cases the evidence of lowered body heat production is not obscure and the patients, while not always presenting a great many symptoms of decreased thyroid function, do show sufficient evidence to warrant study with a view to ruling hypothyroidism in or out. Where this condition is found the administering of thyroid extract is definitely indicated. In Case VI it will be noted that the metabolic rate has remained lowered. This is probably due to the prescribing of an insufficient amount of thyroid, which brings up the very interesting and important question of thyroid dosage.

There is no standard dosage for thyroid extract, and each patient presents his or her own problem as to how much thyroid should be given. Furthermore, the dose established as being adequate at a certain time may in the course of a few weeks prove to be either too great or too small. Most patients in whom thyroid is indicated will probably need it always in varying amounts, and in order to intelligently increase or decrease the dosage to meet the patient's need during any given period there must be periodic clinical observations and studies of the metabolic rate. Many of the so-called therapeutic failures with thyroid, resulting in condemnation of its efficacy, are undoubtedly due to neglect either by the patient or the physician, in adhering to the principle of repeated clinical observations and metabolic rate studies.

FAMILIAL LOW METABOLISM

There is some evidence in our work suggesting that low metabolic states may run in families. The following examples are of interest:

Case IV.—This patient is one of a family of two daughters who are very dissimilar in type of build and general physical and mental characteristics. The patient is said to resemble her father. It so happens that the father is one of three brothers, all of whom presented the following history: (1) Easy fatigue, coming on after the age of thirty-five. (2) Lack of ambition and particularly lack of interest in their chosen profession. This assumed such proportions that two of the brothers retired from business at the age of forty-five. (3) The patient's father felt that there must be some cause for this definite phenomenon, and consequently went to a local sanitarium for study. Here it was found that he had a lowered basal rate and that all other examinations were normal. Thyroid medication has given very beneficial results. Incidentally, it was because of the father's interest in the general subject that the daughter was sent to a physician for basal metabolism studies.

Case V.—This boy has four sisters, all of whom present the following symptoms which are briefly enumerated as follows: (1) An abnormal reaction to cold. (2) Practically no perspiration. (3) Hair coarse and dry. (4) Very sleepy at all times. (5) Mental processes rather slow. (6) Much prefers to sit around than to do anything. Not even interested in carrying on an ordinary conversation. Unfortunately the metabolic study of the family is incomplete, but in the one sister studied there was found a mild degree of secondary anemia and a basal metabolic rate of minus 16 per cent.

The above examples suggest that in any case of a lowered rate a careful inquiry into the family history may give interesting results.

DISCUSSION

It is with some hesitancy that this subject has been presented owing to the fear of creating a wrong impression. Not every patient who presents himself complaining of feeling below par needs to have a metabolism test; nor are we justified in giving thyroid in every instance of a slightly lowered basal metabolic rate. Our position may be briefly stated as follows: According

to present ideas of what is normal and abnormal in basal metabolism readings, a large number of patients have metabolic rates slightly below normal and yet do not present the clinical picture of myxedema. If, however, these patients have any of the symptoms of a lowered heat production, and if a careful physical and laboratory examination reveals no cause of a lowered metabolic rate, then we feel that it is fair to classify such patients as cases of mild hypothyroidism and to try the effect of small doses of thyroid, provided the patient will submit to periodic clinical metabolic checks. We believe that such a standard absolves us from the criticism of using thyroid empirically and at the same time protects the patient from any harmful drug effects.

Of course, after all is said and done, we know very little about what is the normal basal metabolic rate. It is conceivable that some people normally have a low basal metabolism just as some normally have a low blood-pressure or a low pulse rate. About the only way to answer such a question is to metabolize everybody in a large community. Were it possible to do metabolism tests on every individual in a community, and to analyze the results with the corresponding physical findings and personal characteristics, much more could be learned about the significance of basal metabolism readings.

CLINIC OF DR. FRANKLIN W. WHITE

BOSTON CITY HOSPITAL

THE HEALING OF GASTRIC ULCER

THE life history of peptic ulcer is an interesting subject. We are all familiar with its intermittent course and the periods of remission, with absence of symptoms, which may last for months. What happens in these periods of remission? Does the ulcer heal and disappear, or is it present and merely quiescent while the patient is symptom free? Many different opinions have been expressed.

We will show several cases with data bearing on this point, and also upon another interesting question. When a patient has active "ulcer symptoms" including hematemesis, and these symptoms disappear during medical treatment preparatory to operation, and when finally at the end of a month or so an operation is done and no ulcer found, does it mean that no ulcer ever existed and that the hematemesis and other symptoms were due to some other cause? Or, may the ulcer have healed rapidly during this period and disappeared, leaving little or no trace at the end of a month or so?

Since the Roentgen ray with other clinical tests has been used freely to follow the course of gastric ulcers and many resections have been done, we have obtained data of great interest which throw light on these questions.

This data applies especially to gastric ulcers. It is usually easy in ulcers of the lesser curvature, which give such a characteristic picture in profile, to tell by Roentgen signs whether or not the ulcer is healing. This is much less easy and definite in duodenal and pyloric ulcer.

In lesser curvature ulcer the characteristic deformity caused by the lips and crater of the ulcer may steadily change and disappear. The ulcer lips become flatter, the deep crater fills up and smooths over, until no trace of the ulcer deformity remains. The gastric peristalsis at first overactive, becomes normal, and the pyloric spasm lessens and disappears. These changes coincide with the clinical improvement and cessation of symptoms as a rule.

Hamburger,[1] Crohn,[2] Diamond,[3] and others have called attention to the importance of Roentgen study of the healing of peptic ulcer, but the subject has not received the consideration it deserves. Out of a series of 112 gastric and duodenal ulcers treated in our wards in the last five years, all of which have been carefully studied with the Roentgen ray, there were 17 which were definitely identified as lesser curvature ulcers. Of these, 7 have shown clear anatomic and clinical signs of rapid healing under medical treatment. We will show a few typical cases in this clinic.

Case I.—Mr. C. N., a house painter of fifty-four, had for two years intermittent attacks of hunger pain with food relief and little soda relief. His diet was careless and there was a gradual loss of 20 pounds in two years. There was no earlier bleeding, but the day before admission profuse hematemesis; his hemoglobin was 35 per cent. and red cells 2,300,000. Transfusion was done and he was given the Sippy treatment in bed.

x-Ray examination two weeks after admission showed a medium-sized ulcer in the middle of the lesser curvature with definite lips and crater (Fig. 166); the stomach was empty in five hours after a barium meal. The patient soon became symptom free and gained rapidly on medical treatment.

A second *x*-ray examination four weeks after admission showed that the ulcer defect had entirely disappeared, the lips

[1] Amer. Jour. Med. Sci., 1918, vol. 155, p. 204.
[2] Arch. of Int. Med., 1926, vol. 37, p. 217.
[3] Amer. Jour. Med. Sci., 1922, vol. 163, p. 548.

had flattened out, the crater filled up and only a slight stiffness of the stomach wall was left to mark the spot (Fig. 167).

The immediate results of medical treatment were excellent, but operation was advised on account of the patient's careless habits which made proper dieting unlikely and because of the possibility of another hemorrhage. At operation six weeks after admission, the scar of a healed ulcer was found in the middle of the lesser curvature with only a little induration about

Fig. 166.—Case I. Medium-sized gastric ulcer in the middle of the lesser curvature with clearly defined crater.

it. Excision was done and the patient has remained well for four years.

This case shows the rapid effect of medical treatment in healing a chronic gastric ulcer, which had evidently recurred many times over a long period, but which entirely closed within six weeks of suitable medical care.

It confirms the *x*-ray diagnosis of rapid healing made before operation, and shows the value of this method of examination.

Fig. 167.—Case I. Two weeks later. Ulcer deformity entirely gone. Patient symptom free (seven other films of the stomach taken at this time at all angles, showed no deformity).

Case II.—Mr. M. R. V., a milkman of fifty-four, was always well till three years ago when he began to have irregular attacks of "sour stomach" or pain across the upper abdomen three or four times a day, sometimes a half hour after meals, sometimes with no relation to meals. This was relieved by lying down, but not by soda. There was no night pain. He occasionally vomited, about a half hour after meals, a cupful of partly digested food with no blood or old food.

Two years ago he had a laparotomy with the diagnosis of peptic ulcer, but no ulcer was found. The appendix was removed and two small inguinal hernias were closed.

He was well for a year, but during the past year the same

symptoms have recurred, getting gradually worse. He has eaten a "careful diet" including raw vegetables and raw fruit, and has lost in weight from 145 to 125 pounds. He has no lower teeth and smokes 20 cigarettes a day. His gastric contents one hour after a test breakfast showed free acid 35, total acidity 70, no mucus or blood.

One week before we saw him a diagnosis of gastric ulcer was made, and he was put on a modified Sippy régime with rapid

Fig. 168.—Case II. One week later. Ulcer deformity practically gone. There was slight stiffness of the middle of the lesser curvature. (This is one of a series of six films; all alike.)

relief of symptoms. Our first *x*-ray examination showed practically normal gastric peristalsis and nothing abnormal in gastric contours, except a very slight inconstant irregularity near the middle of the lesser curvature, with a slightly lessened flexibility at this point (Fig. 168). No one could have diagnosed a gastric ulcer from these plates.

The diagnosis was not made clear until the plates taken one

week *before* (by Dr. E. L. Davis of Springfield, Mass.) were sent for, which showed a typical ulcer of moderate size about the middle of the lesser curvature (Fig. 169). Peristalsis was very active, and marked pyloric spasm was present. The stomach emptied in six hours, however.

He has continued on ambulatory medical treatment of the ulcer for the last seven months, with no return of symptoms or of ulcer deformity. We expect to make this healing permanent.

Fig. 169.—Case II. Medium-sized gastric ulcer on the lesser curvature at the beginning of medical treatment.

This case illustrates the rapid disappearance of a gastric ulcer within a week or two on medical treatment. It is especially interesting to note that this patient had the same symptoms two years before, and after a brief course of medical treatment no ulcer was found at operation. It probably healed rapidly during this time and was unrecognizable at operation.

Case III.—Mr. J. R. S., a business man of forty-five, has had for two years attacks of epigastric distress coming two or three

hours after meals with a little nausea, but no vomiting or actual pain. The attacks lasted about a month, with intermissions of two or three months. He has been relieved by alkaline tablets, and has eaten a general diet. He smokes one or two cigars and eight or ten cigarettes a day. He has always been rather thin, weighing 130 to 135 pounds (average for age and height 165 pounds), but there has been no loss of weight. One infected tooth had been removed four days ago.

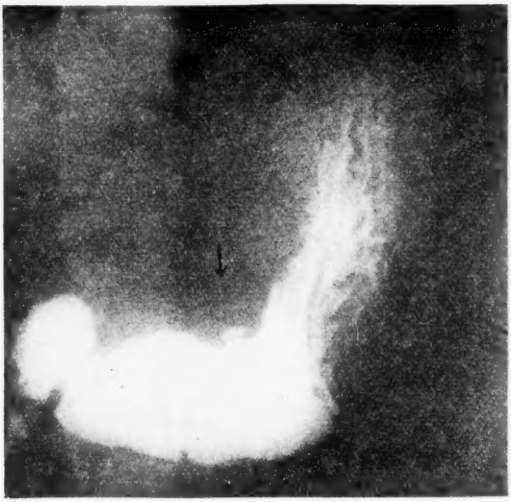

Fig. 170.—Case III. Medium-sized gastric ulcer on the lesser curvature at the beginning of medical treatment.

He has some pyorrhea, active reflexes, and an undescended right testicle. His gastric contents one hour after a test breakfast showed free acid 50, total acidity 62, no mucus or blood. The feces showed no occult blood with benzidin. *x*-Ray examination showed moderate ptosis and a good-sized ulcer about 2 inches in total diameter, with crater, near the middle of the lesser curvature (Fig. 170). Gastric peristalsis was rather sluggish, the tone low, the duodenum was normal. There was a 25 per cent. gastric residue six hours after a barium meal.

He was put to bed for a week on a modified Sippy régime with 4 or 5 alkaline powders daily and 1/150 grain of atropin sulphate twice a day. His symptoms disappeared within a week and he gained weight steadily.

x-Ray examination five days later showed a slight change. The ulcer was a little flatter and the crater less deep (Fig. 171). An *x*-ray one month later showed a marked change; the ulcer deformity was about gone with only a trace of the crater remaining (Fig. 172). The stomach emptied completely within

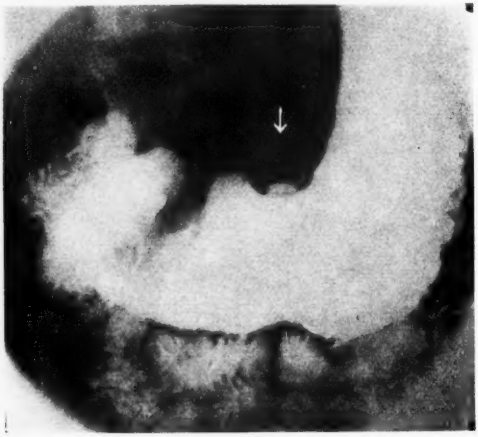

Fig. 171.—Case III. Five days later; slight change; ulcer a little flatter, crater less deep.

six hours. An *x*-ray six months later showed the ulcer deformity entirely gone (Fig. 173).

The clinical course ran parallel with the *x*-ray findings, his symptoms practically disappeared within a week, and he has remained well for the last three years, and gained steadily in weight: 131 pounds at the beginning of treatment, 142 in a month, 152 in two months, 158 in six months, and 170 three years later.

This patient was put on medical treatment on account of his good general condition, lack of complications, and rather mild symptoms. This case is a good example of the gradual complete

Fig. 172.—Case III. One month later; marked change; ulcer deformity almost gone, a trace of the crater remains.

Fig. 173.—Case III. Six months later; ulcer deformity entirely gone; patient well for five months (and has continued well for three years).

healing of a lesser curvature ulcer of good size, and the *x*-rays illustrate how accurately the gradual disappearance of the ulcer itself can be followed by this method.

Before speaking of what we have learned from these cases, let us first dispose of any objections which might be raised to the medical study or treatment of gastric ulcer on account of the risk of serious complications. We began our medical treatment with a healthy fear of the possibilities of cancer, but were encouraged by the present opportunities to see what is happening to the ulcer by means of the *x*-ray, and by the rapid disappearance of many gastric ulcers under medical treatment in four to six weeks, and by finding that cancer developing on our gastric ulcers was a rarity, approximately 2 per cent. in a large series of cases followed for three to five years. We were left with the impression that nearly all cancers supposed to develop from chronic ulcer have been malignant from the start.

Any physician who attempts medical treatment or study of gastric ulcer must do it with his eyes open and with a due sense of responsibility and a willingness to follow his cases with painstaking care by clinical study, by *x*-ray examination, blood tests of feces and stomach contents and tests of the emptying of the stomach. If this is done such treatment and study is reasonable and safe, favorable cases are continued on medical treatment and unfavorable ones weeded out and referred to the surgeon.

We have had no serious mistakes under this scheme, no serious complications and no unexpected cancer developing on our ulcers under continued medical treatment.

The points which we wish to emphasize in studying these cases are as follows:

(1) The pictures of lesser curvature ulcers under medical treatment speak for themselves and show how accurately the healing and disappearance of the ulcer may be followed by means of the Roentgen ray. Case I is typical of several we have seen and more that have been reported by Crohn, in which the disappearance of the anatomic ulcer seen by the *x*-ray has been verified by operation, thus putting the conclusions from the *x*-ray examination on a definite and reliable footing.

It is needless to say that these changes must be carefully correlated with changes in symptoms and other physical signs.

Occasionally the *x*-ray signs may be more important than the clinical. The patient may lose his symptoms and gain weight, but lack of healing shown by the *x*-ray may give the best indication of a severe lesion. The best time for the re-examination of the stomach is at the end of one or two weeks after treatment has begun, again after one or two months, and at some later periods.

There is some objection to *x*-ray studies of local deformity as an index of the healing of an ulcer. The crater may fill with food or mucus and appear healed, or the stomach may be rotated a little at subsequent examinations and the ulcer hidden. These objections call for careful work and interpretation, but are not serious. This *x*-ray evidence of the rapid healing of gastric ulcer has been checked up by operation as already mentioned in several of our cases and found to be an actual fact.

(2) The rapid healing of gastric ulcer in these cases indicates that in many other cases when the patient is symptom free the ulcer is not present and simply quiescent, but has actually disappeared. In gross appearance we might even compare the active ulcer to a boil with much irritation and infection and much round-cell infiltration and swelling. In a month or so we find the swelling all gone, the crater filled up, the ulcer flat, and little but scar tissue left.

(3) In selecting the types of gastric ulcer which we may expect to heal with medical treatment we think first of the absence of complications such as recurrent bleeding, persistent obstruction, and of course perforation.

The *age of the patient* is also important, the younger ones do better. We get a decidedly higher percentage of medical cures in patients under forty-five than over. The cases with permanent craters are usually over forty and mostly over fifty.

The *size of the ulcer* and the *duration of symptoms* and the *length of the intermissions* are important. The larger and deeper ulcers usually cause severe continuous symptoms, and we find the small and moderate-sized ulcers where there are short histories, short attacks, and long intermissions, the so-called acute recurrent type of ulcer. These give us our best medical results,

and if the intermissions are more than six weeks long there is the greatest tendency to heal.

We expect the crater to disappear in about 50 per cent. of the lesser curvature ulcers in from one to two months' time on the average. The cases with persistent craters are usually over forty-five.

It is important to have intelligent patients, who are willing to see the doctor occasionally during a period of several years when symptom free. We can make medical treatment a success with a larger proportion of private than hospital patients because of their greater intelligence, easier circumstances, better food, and better contact with the physician.

To summarize, the younger the patient, the shorter the whole course of symptoms, the longer the intermissions and the smaller the ulcer, and the better the co-operation of the patient the better the chance of healing under medical treatment. On the other hand, the ulcers of large size, of gradual onset, and long duration usually have almost continuous symptoms and are nearly always surgical. We expect final medical healing in about one-half the lesser curvature ulcers and surgery in about one-half.

(4) It also seems probable that some cases of so-called "essential hematemesis," in which no peptic ulcer is found at operation, are actual cases of gastric ulcer which have healed rapidly on good medical treatment, and have entirely disappeared in the period of three or four or six weeks which has elapsed between the time of the hematemesis and the time of operation. An operation may be done at a period in the life-cycle of any acute recurrent ulcer when rapid healing has obliterated the crater, and made it difficult or impossible to find by the surgeon.